

# Search history

Ghali 10/019121

07/07/2006

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(FILE 'HOME' ENTERED AT 09:05:37 ON 07 JUL 2006).

FILE 'REGISTRY' ENTERED AT 09:05:49 ON 07 JUL 2006

FILE 'HCAPLUS' ENTERED AT 09:06:06 ON 07 JUL 2006

E US2003-19121/APPS

L1

1 SEA ABB=ON PLU=ON US2003-19121/APPS  
D IALL

FILE 'STNGUIDE' ENTERED AT 09:07:04 ON 07 JUL 2006

FILE 'HCAPLUS' ENTERED AT 09:12:37 ON 07 JUL 2006  
SEL RN

FILE 'REGISTRY' ENTERED AT 09:12:48 ON 07 JUL 2006

L2

15 SEA ABB=ON PLU=ON (103775-10-6/BI OR 198292-69-2/BI OR  
5333-42-6/BI OR 7631-86-9/BI OR 82834-16-0/BI OR 83647-97-6/BI  
OR 86541-75-5/BI OR 87269-97-4/BI OR 87333-19-5/BI OR 87679-37-  
6/BI OR 87679-71-8/BI OR 88768-40-5/BI OR 89371-37-9/BI OR  
9015-82-1/BI OR 98048-97-6/BI)

D SCA

E ANGIOTENSIN/CN

L3

8 SEA ABB=ON PLU=ON ANGIOTENSIN CONVERTING ENZYME?/CN  
D SCA

L4

1 SEA ABB=ON PLU=ON ANGIOTENSIN CONVERTING ENZYME INHIBITORY?/C  
N

L5

1 SEA ABB=ON PLU=ON 9015-82-1  
D SCA

L6

0 SEA ABB=ON PLU=ON L3 AND L5  
E ANGIOTENSIN-CONVERTING/CN

L7

17 SEA ABB=ON PLU=ON ANGIOTENSIN-CONVERTING ENZYME?/CN

L8

23 SEA ABB=ON PLU=ON L7 OR L3

L\*\*\* DEL

1 S L8 AND L5  
D COST

FILE 'HCAPLUS' ENTERED AT 09:24:38 ON 07 JUL 2006

L9

16578 SEA ABB=ON PLU=ON L8

L10

10345 SEA ABB=ON PLU=ON L8 (L) INHIB?/OBI  
E ACE+ALL/CT  
E ACE INHIB?

L11

9707 SEA ABB=ON PLU=ON (ANGIOTENSIN CONVERTING ENZYM?/OBI OR  
ACE/OBI) (1A) INHIB?/OBI

FILE 'STNGUIDE' ENTERED AT 09:28:48 ON 07 JUL 2006

FILE 'REGISTRY' ENTERED AT 09:30:29 ON 07 JUL 2006

E IMIDAPRIL/CN

L12

3 SEA ABB=ON PLU=ON IMIDAPRIL?/CN  
E FOSINOPRIL/CN

L13

4 SEA ABB=ON PLU=ON FOSINOPRIL?/CN  
E MOEXIPRIL/CN

L14

3 SEA ABB=ON PLU=ON MOEXIPRIL?/CN  
E PERINDOPRIL/CN

L15

8 SEA ABB=ON PLU=ON PERINDOPRIL?/CN  
D SCA

E RAMIPRIL/CN

L16

5 SEA ABB=ON PLU=ON RAMIPRIL?/CN  
E SPIRAPRIL/CN

L17 3 SEA ABB=ON PLU=ON SPIRAPRIL?/CN  
 D SCA  
 E CILAZIPRIL/CN  
 E CILAZAPRIL/CN  
 L18 6 SEA ABB=ON PLU=ON CILAZAPRIL?/CN  
 E BENAZEPRIL/CN  
 L19 5 SEA ABB=ON PLU=ON BENAZEPRIL?/CN  
 E TRANDOLAPRIL/CN  
 L\*\*\* DEL 1 S TRANDOLAPRIL/CN  
 L20 4 SEA ABB=ON PLU=ON TRANDOLAPRIL?/CN  
 L21 41 SEA ABB=ON PLU=ON (L12 OR L13 OR L14 OR L15 OR L16 OR L17 OR  
 L18 OR L19 OR L20)  
 SAVE TEMP L21 GHA121PRILS/A

FILE 'HCAPLUS' ENTERED AT 09:41:27 ON 07 JUL 2006

L22 3797 SEA ABB=ON PLU=ON L21  
 L23 152437 SEA ABB=ON PLU=ON DRUG DELIVERY SYSTEMS/CT  
 L24 6516 SEA ABB=ON PLU=ON L23 (L) TRANSDERM?/OBI  
 L25 27 SEA ABB=ON PLU=ON L22 AND L24  
 D SCA

FILE 'STNGUIDE' ENTERED AT 09:45:13 ON 07 JUL 2006

FILE 'REGISTRY' ENTERED AT 09:54:39 ON 07 JUL 2006

L26 1 SEA ABB=ON PLU=ON EUTANOL G/CN  
 L27 1 SEA ABB=ON PLU=ON SILICON DIOXIDE/CN  
 L28 1 SEA ABB=ON PLU=ON 198292-69-2  
 D SCA  
 D IDE  
 L\*\*\* DEL 2 S L26-L27 AND L2

FILE 'HCAPLUS' ENTERED AT 09:57:43 ON 07 JUL 2006

L29 77 SEA ABB=ON PLU=ON (L10 OR L11 OR L22) AND L24  
 L30 35415 SEA ABB=ON PLU=ON MEDICAL GOODS/CT  
 L31 12 SEA ABB=ON PLU=ON L29 AND L30  
 D SCA  
 L32 4111 SEA ABB=ON PLU=ON L30 (L) (PLASTER?/OBI OR TOPICAL?/OBI OR  
 ADHESIV?/OBI OR BANDAG?/OBI)  
 L33 6 SEA ABB=ON PLU=ON L31 AND L32  
 D SCA  
 L34 4 SEA ABB=ON PLU=ON L29 AND ((L26 OR L27))  
 D SCA  
 L\*\*\* DEL 9 S L33-L34  
 L35 1707 SEA ABB=ON PLU=ON PERMEATION ENHANCERS/CT  
 L36 8 SEA ABB=ON PLU=ON L29 AND L35  
 D SCA  
 L37 225267 SEA ABB=ON PLU=ON ADHESIV?/BI  
 L38 6 SEA ABB=ON PLU=ON L36 AND L37  
 D SCA  
 L\*\*\* DEL 13 S L33-L34 OR L38  
 L39 48687 SEA ABB=ON PLU=ON PATCH?/BI  
 L40 9 SEA ABB=ON PLU=ON L39 AND L29  
 D SCA  
 L41 13 SEA ABB=ON PLU=ON L33 OR L34 OR L38  
 L42 21 SEA ABB=ON PLU=ON L41 OR L40  
 L43 185223 SEA ABB=ON PLU=ON MATRIX/OBI OR MATRIC?/OBI  
 L44 4 SEA ABB=ON PLU=ON L29 AND L43  
 D SCA  
 L45 24 SEA ABB=ON PLU=ON L42 OR L44  
 E MEDICAL GOODS/CT

E E67+ALL  
 L46 10102 SEA ABB=ON PLU=ON PLASTER?/OBI  
 L47 2 SEA ABB=ON PLU=ON L29 AND L46  
 D SCA  
 L48 14644 SEA ABB=ON PLU=ON PLASTER?/BI  
 L49 2 SEA ABB=ON PLU=ON L48 AND L29  
 L50 26 SEA ABB=ON PLU=ON KLOKKERS K?/AU  
 L51 897 SEA ABB=ON PLU=ON KRAMER K?/AU  
 L52 2531 SEA ABB=ON PLU=ON FISCHER W?/AU  
 E SENDL/AU  
 L53 11 SEA ABB=ON PLU=ON SENDL A?/AU  
 L54 6 SEA ABB=ON PLU=ON SENDL LANG A?/AU  
 L\*\*\* DEL 5 S L5 AND (L51-L54)  
 L55 16 SEA ABB=ON PLU=ON L50 AND ((L51 OR L52 OR L53 OR L54))  
 L56 1 SEA ABB=ON PLU=ON L51 AND (L52 OR L53 OR L54)  
 L57 6 SEA ABB=ON PLU=ON L52 AND (L53 OR L54)  
 L\*\*\* DEL 20 S L55-L57  
 L58 20 SEA ABB=ON PLU=ON (L55 OR L56 OR L57)  
 E PHARMACEUTICAL DOSAGE FORMS/CT  
 E E220+ALL/CT  
 L59 48095 SEA ABB=ON PLU=ON PHARMACEUTICAL DOSAGE FORMS/CT  
 L60 5248 SEA ABB=ON PLU=ON L59 (L) (TRANSERM?/OBI OR PLASTER?/OBI OR  
 TOPICAL?/OBI OR ADHESIV?/OBI OR BANDAG?/OBI)  
 L61 13 SEA ABB=ON PLU=ON (L10 OR L11 OR L22) AND L60  
 D SCA  
 L62 QUE ABB=ON PLU=ON SALT?/OBI OR ESTER?/OBI OR ACID?/OBI  
 L63 10 SEA ABB=ON PLU=ON L61 AND L62  
 L64 QUE ABB=ON PLU=ON SALT?/CW  
 L65 QUE ABB=ON PLU=ON ESTER?/OBI  
 L66 QUE ABB=ON PLU=ON ACID?/CW  
 L67 QUE ABB=ON PLU=ON BASE?/OBI  
 L68 6 SEA ABB=ON PLU=ON L61 AND (L64 OR L65 OR L66 OR L67)  
 D SCA  
  
 FILE 'MEDLINE' ENTERED AT 10:56:50 ON 07 JUL 2006  
 L69 0 SEA ABB=ON PLU=ON KLOKKERS K?/AU  
 E KLOKKERS/AU  
 E KLOKKER/AU  
 L70 556 SEA ABB=ON PLU=ON KRAMER K?/AU  
 L71 931 SEA ABB=ON PLU=ON FISCHER W?/AU  
 E SENDL/AU  
 L72 7 SEA ABB=ON PLU=ON SENDL A?/AU  
 E SENDL LAN/AU  
 L73 0 SEA ABB=ON PLU=ON (L70 OR L71) AND L72  
 E ANGIOTENSIN-CONVERTING ENZYME INHIBITORS+ALL/CT  
 L74 30261 SEA ABB=ON PLU=ON ANGIOTENSIN-CONVERTING ENZYME INHIBITORS+NT  
 /CT  
 L75 4016 SEA ABB=ON PLU=ON L21  
 L\*\*\* DEL 3901 S L74 AND L75  
 L\*\*\* DEL 4016 S L75-L76  
 L76 30376 SEA ABB=ON PLU=ON (L74 OR L75)  
 D COST

FILE 'STNGUIDE' ENTERED AT 11:02:41 ON 07 JUL 2006

FILE 'MEDLINE' ENTERED AT 11:03:45 ON 07 JUL 2006

E ADMINISTRATION, CUTANEOUS+ALL/CT  
 L77 8710 SEA ABB=ON PLU=ON ADMINISTRATION, CUTANEOUS/CT  
 L78 23 SEA ABB=ON PLU=ON L76 AND L77  
 D TRIAL 1-23

L79 200468 SEA ABB=ON PLU=ON ADHESIV? OR ADHESION? OR ADHERE?  
 L80 43255 SEA ABB=ON PLU=ON SILICON?  
 L81 QUE ABB=ON PLU=ON ESTER? OR SALT? OR PRODRUG? OR BASE? OR  
 ACID?  
 L82 QUE ABB=ON PLU=ON (PERMEAT? OR PENETRAT?) (W) ENHANC?  
 L83 QUE ABB=ON PLU=ON BANDAG?  
 L84 QUE ABB=ON PLU=ON PATCH?  
 L85 QUE ABB=ON PLU=ON MATRIX? OR MATRIC?  
 L86 QUE ABB=ON PLU=ON L26 OR L27  
 L87 11 SEA ABB=ON PLU=ON L78 AND (L79 OR L80 OR L81 OR L82 OR L83  
 OR L84 OR L85)  
 D TRIAL 1-11  
 L88 1 SEA ABB=ON PLU=ON (L69 OR L70 OR L71 OR L72) AND L76  
 L89 1 SEA ABB=ON PLU=ON (L69 OR L70 OR L71 OR L72) AND L77  
 L90 4200 SEA ABB=ON PLU=ON PLASTER?  
 L91 0 SEA ABB=ON PLU=ON L78 AND L90

FILE 'EMBASE' ENTERED AT 11:17:21 ON 07 JUL 2006

E ANGIOTENSIN-CONVERTING ENZYME INHIBITORS+ALL/CT

E DIPEPTIDYL CARBOXYPEPTIDASE INHIBITOR+ALL/CT

L92 69828 SEA ABB=ON PLU=ON DIPEPTIDYL CARBOXYPEPTIDASE INHIBITOR+NT/CT

L93 2 SEA ABB=ON PLU=ON KLOKKERS K?/AU

L94 386 SEA ABB=ON PLU=ON KRAMER K?/AU

L95 664 SEA ABB=ON PLU=ON FISCHER W?/AU

L\*\*\* DEL 9 S SENDL A/AU

L\*\*\* DEL 11 S SENDL A?/AU

L96 11 SEA ABB=ON PLU=ON SENDL A?/AU

L97 0 SEA ABB=ON PLU=ON SENDL LANG A?/AU

L\*\*\* DEL 0 S SENDL-LANG A?/AU

L98 0 SEA ABB=ON PLU=ON L93 AND (L94 OR L95 OR L96)

L99 0 SEA ABB=ON PLU=ON L94 AND (L95 OR L96)

L100 0 SEA ABB=ON PLU=ON L95 AND L96

L101 1 SEA ABB=ON PLU=ON L92 AND (L93 OR L94 OR L95 OR L96 OR L97)

D TRIAL

L102 11458 SEA ABB=ON PLU=ON L21

L103 12386 SEA ABB=ON PLU=ON (L26 OR L27)

D COST

FILE 'STNGUIDE' ENTERED AT 12:09:17 ON 07 JUL 2006

FILE 'EMBASE' ENTERED AT 12:46:08 ON 07 JUL 2006

L\*\*\* DEL 0 S L102 (L) (TP OR TD)/CT

L\*\*\* DEL 0 S L21 (L) AD/CT

L104 0 SEA ABB=ON PLU=ON L92 (L) (TP OR TD)/CT

L105 11 SEA ABB=ON PLU=ON L92 (L) (TP OR TD)/CT

D TRIAL 1-11

E TRANSDERMAL DRUG ADMINISTRATION+ALL/CT

L106 11038 SEA ABB=ON PLU=ON TRANSDERMAL DRUG ADMINISTRATION/CT

E TOPICAL DRUG ADMINISTRATION/CT

E TOPICAL DRUG ADMINISTRATION/CT

E E4=ALL

E TOPICAL DRUG ADMINISTRATION/CT

E E4+ALL

L107 88500 SEA ABB=ON PLU=ON TOPICAL DRUG ADMINISTRATION/CT

L108 894 SEA ABB=ON PLU=ON (L106 OR L107) AND (L92 OR L102)

D TRIAL 1-5

L109 304 SEA ABB=ON PLU=ON L108 NOT ((TD OR TP)/CT)

D TRIAL 1-5

D TRIAL 6-10

L110 590 SEA ABB=ON PLU=ON L108 NOT L109  
 D TRIAL 1-5  
 L111 377 SEA ABB=ON PLU=ON IMIDAPRIL  
 D TRIAL 1-5  
 L112 1707 SEA ABB=ON PLU=ON FOSINOPRIL  
 L113 238 SEA ABB=ON PLU=ON MOEXIPRIL  
 D TRIAL  
 E MOEXIPRIL/CT  
 L\*\*\* DEL 3045 S PERINDOPRIL/CT  
 L\*\*\* DEL 4985 S RAMIPRIL/CT  
 L\*\*\* DEL 5051 S RAMIPRIL  
 L114 3094 SEA ABB=ON PLU=ON PERINDOPRIL  
 L115 5051 SEA ABB=ON PLU=ON RAMIPRIL  
 L116 266 SEA ABB=ON PLU=ON SPIRAPRIL  
 L117 1403 SEA ABB=ON PLU=ON CILAZAPRIL  
 L118 1406 SEA ABB=ON PLU=ON BENAZEPRIL  
 L119 1693 SEA ABB=ON PLU=ON TRANDOLAPRIL  
 L120 1 SEA ABB=ON PLU=ON ((L111 OR L112 OR L113 OR L114 OR L115 OR  
 L116 OR L117 OR L118 OR L119)) (L) (TP OR TD)/CT  
 D TRIAL  
 E TRANDOLIPRIL  
 E E4+ALL  
 L121 1722 SEA ABB=ON PLU=ON TRANDOL!PR!L##  
 L122 29 SEA ABB=ON PLU=ON L121 NOT L119  
 D TRIAL  
 L123 427 SEA ABB=ON PLU=ON RAMIPRILAT  
 L124 391 SEA ABB=ON PLU=ON IMIDAPRIL##  
 L\*\*\* DEL 14 S L124 NOT L111  
 D TRIAL 1-3  
 L125 1748 SEA ABB=ON PLU=ON FOSIN!PRIL##  
 E MOEX!PRIL##  
 L126 253 SEA ABB=ON PLU=ON MOEX!PRIL##  
 L127 3220 SEA ABB=ON PLU=ON PERIND!PRIL##  
 L128 5309 SEA ABB=ON PLU=ON RAM!PRIL##  
 L129 281 SEA ABB=ON PLU=ON SPIR!PRIL##  
 L130 1461 SEA ABB=ON PLU=ON CILAZ!PRIL##  
 L131 1496 SEA ABB=ON PLU=ON BENAZ!PRIL##  
 L132 1723 SEA ABB=ON PLU=ON TRAND!L!PRIL##  
 L133 1 SEA ABB=ON PLU=ON (L123 OR L124 OR L125 OR L126 OR L127 OR  
 L128 OR L129 OR L130 OR L131 OR L132) (L) (TP OR TD)/CT  
 D TRIAL  
 D TRIAL L105 1-11  
 L134 1570 SEA ABB=ON PLU=ON DRUG ADMINISTRATION ROUTE  
 L135 1 SEA ABB=ON PLU=ON L105 AND L134  
 D TRIAL  
 L136 19958 SEA ABB=ON PLU=ON ADHESIV?  
 L137 1 SEA ABB=ON PLU=ON L105 AND L136  
 D TRIAL  
 L138 9222 SEA ABB=ON PLU=ON DRUG PENETRATION  
 L139 3 SEA ABB=ON PLU=ON L105 AND L138  
 D TRIAL 1-3  
 L140 69918 SEA ABB=ON PLU=ON L92 OR L102 OR (L123 OR L124 OR L125 OR  
 L126 OR L127 OR L128 OR L129 OR L130 OR L131 OR L132)  
 D TRIAL 1-3  
 L141 25 SEA ABB=ON PLU=ON L140 AND L134  
 D TRIAL 1-6  
 L142 4 SEA ABB=ON PLU=ON L141 AND (L106 OR L107)  
 D TRIAL 1-4  
 L143 0 SEA ABB=ON PLU=ON L102 (L) (TP OR TD)/CT  
 L144 895 SEA ABB=ON PLU=ON L140 AND (L106 OR L107)

L145 305 SEA ABB=ON PLU=ON L144 NOT ((TP OR TD)/CT)  
 D TRIAL  
 D TRIAL 1-5  
 L146 0 SEA ABB=ON PLU=ON L103 AND L145  
 L147 38087 SEA ABB=ON PLU=ON SILICON?  
 L148 1 SEA ABB=ON PLU=ON L145 AND L147  
 D TRIAL  
 L\*\*\* DEL QUE PATCH  
 L149 QUE ABB=ON PLU=ON PATCH?  
 L150 QUE ABB=ON PLU=ON MATRIX? OR MATRIC?  
 L151 QUE ABB=ON PLU=ON BANDAG?  
 L152 QUE ABB=ON PLU=ON (PERMEAT? OR PENETRAT?) (1A) ENHANC?  
 L153 QUE ABB=ON PLU=ON PRODRUG?  
 L154 QUE ABB=ON PLU=ON ADHESIV?  
 L155 QUE ABB=ON PLU=ON PLASTER?  
 L156 QUE ABB=ON PLU=ON ESTER?  
 L157 QUE ABB=ON PLU=ON SALT?  
 L158 QUE ABB=ON PLU=ON BASE OR BASES  
 L159 QUE ABB=ON PLU=ON ACID OR ACIDIC  
 L160 137 SEA ABB=ON PLU=ON L145 AND (L149 OR L150 OR L151 OR L152 OR  
 L153 OR L154 OR L155 OR L156 OR L157 OR L158 OR L159)  
 D TRIAL 1  
 D TRIAL 1-5  
 L161 18 SEA ABB=ON PLU=ON L145 AND L149  
 D TRIAL 1-18  
 L\*\*\* DEL 0 S TRANSDERMAL DRUG ADMINISTRATION/MAJ  
 L162 11038 SEA ABB=ON PLU=ON TRANSDERMAL DRUG ADMINISTRATION/CT  
 L163 3870 SEA ABB=ON PLU=ON L162/MAJ  
 L164 1 SEA ABB=ON PLU=ON L161 AND L163  
 D TRIAL  
 L165 4 SEA ABB=ON PLU=ON L145 AND L150  
 D TRIAL 1-4  
 L166 0 SEA ABB=ON PLU=ON L145 AND L151  
 L167 0 SEA ABB=ON PLU=ON L145 AND L152  
 L168 2 SEA ABB=ON PLU=ON L144 AND L152  
 D TRIAL 1-2  
 L\*\*\* DEL 590 S L144 (L) (TP OR TD)/CT  
 D TRIAL 1-15  
 L169 6 SEA ABB=ON PLU=ON L145 AND L153  
 D TRIAL 1-6  
 L170 2894 SEA ABB=ON PLU=ON SKIN PERMEABILITY  
 L171 1 SEA ABB=ON PLU=ON L169 AND L170  
 D TRIAL  
 L172 0 SEA ABB=ON PLU=ON L145 AND L154  
 L173 2 SEA ABB=ON PLU=ON L144 AND L154  
 D TRIAL 1-2  
 L174 0 SEA ABB=ON PLU=ON L145 AND L155  
 L175 0 SEA ABB=ON PLU=ON L144 AND L155  
 L176 2 SEA ABB=ON PLU=ON L145 AND L158  
 D TRIAL  
 D TRIAL 2  
 L177 1 SEA ABB=ON PLU=ON GEL AND L176  
 L178 7 SEA ABB=ON PLU=ON L156 AND L145  
 D TRIAL 1-7  
 L179 2 SEA ABB=ON PLU=ON L178 AND L170  
 D TRIAL 1-2  
 L180 2 SEA ABB=ON PLU=ON L102 AND L103  
 D TRIAL 1-2

FILE 'BIOSIS' ENTERED AT 13:53:17 ON 07 JUL 2006

L181 5806 SEA ABB=ON PLU=ON (L124 OR L125 OR L126 OR L127 OR L128 OR  
L129 OR L130 OR L131 OR L132)  
E DIPEPTIDYL CARBOXYPEPTIDASE INHIBITOR/CT  
E ACE INHIBITOR+ALL/CT  
E E3+ALL  
E ANGIOTENSIN CONV/CT

L182 1190 SEA ABB=ON PLU=ON ANGIOTENSIN CONVERTING ENZYME INHIBITOR/CT

L183 9251 SEA ABB=ON PLU=ON ACE INHIBITOR?

L184 7150 SEA ABB=ON PLU=ON TRANSDERMAL

L185 0 SEA ABB=ON PLU=ON L184 AND L182

L186 14 SEA ABB=ON PLU=ON L184 AND L183  
D SCA

L\*\*\* DEL 0 S TRANSDERM? (W) ADMINISTR?

L187 1573 SEA ABB=ON PLU=ON TRANSDERM? (W) ADMINISTR?

L188 5 SEA ABB=ON PLU=ON L186 AND L187  
D SCA

L189 148 SEA ABB=ON PLU=ON (TRANSDERM? (W) ADMINISTR? )/TI

L190 2 SEA ABB=ON PLU=ON L189 AND L188

L191 QUE ABB=ON PLU=ON PATCH? OR PLASTER? OR ADHESIV? OR BANDAG?  
OR SILICON? OR MATRIX? OR MATRIC? OR ((PENETRAT? OR PERMEAT?)  
(W) ENHANC?)

L192 3 SEA ABB=ON PLU=ON L186 AND L191  
D SCA

L193 256 SEA ABB=ON PLU=ON (L181 OR L182 OR L183) AND L191

L194 1348 SEA ABB=ON PLU=ON (TRANSDERM? OR TOPICAL?) (S) PATCH?

L195 2 SEA ABB=ON PLU=ON L193 AND L194  
D SCA

L196 2 SEA ABB=ON PLU=ON (L181 OR L182 OR L183) AND L194  
D SCA  
D COST

FILE 'STNGUIDE' ENTERED AT 14:04:13 ON 07 JUL 2006

FILE 'EMBASE' ENTERED AT 14:04:18 ON 07 JUL 2006

L197 1 SEA ABB=ON PLU=ON (L93 OR L94 OR L95 OR L96 OR L97) AND L140

L198 2 SEA ABB=ON PLU=ON (L93 OR L94 OR L95 OR L96 OR L97) AND L162

L199 1 SEA ABB=ON PLU=ON (L93 OR L94 OR L95 OR L96 OR L97) AND L92

FILE 'BIOSIS' ENTERED AT 14:06:19 ON 07 JUL 2006

L200 15 SEA ABB=ON PLU=ON KLOKKERS K?/AU

L201 812 SEA ABB=ON PLU=ON KRAMER K?/AU

L\*\*\* DEL 0 S FISCHERW?/AU

L202 881 SEA ABB=ON PLU=ON FISCHER W?/AU

L\*\*\* DEL 81 S SENDL?/AU  
E SENDL?/AU

L203 13 SEA ABB=ON PLU=ON SENDL A?/AU

L204 5 SEA ABB=ON PLU=ON SENDL LANG A?/AU

L205 12 SEA ABB=ON PLU=ON L200 AND (L201 OR L202 OR L203 OR L204)

L206 0 SEA ABB=ON PLU=ON L201 AND (L202 OR L203 OR L204)

L207 5 SEA ABB=ON PLU=ON L202 AND (L203 OR L204)

L208 15 SEA ABB=ON PLU=ON (L205 OR L206 OR L207)  
D SCA

FILE 'DRUGU' ENTERED AT 14:10:52 ON 07 JUL 2006

L209 6308 SEA ABB=ON PLU=ON (L124 OR L125 OR L126 OR L127 OR L128 OR  
L129 OR L130 OR L131 OR L132)

L210 19007 SEA ABB=ON PLU=ON ACE INHIBITOR?

L211	2457	SEA ABB=ON	PLU=ON	ANGIOTENSIN CONVERTING ENZYME INHIBITOR
L212	8522	SEA ABB=ON	PLU=ON	PATCH?
		D SCA		
		D TRIAL 1-45		
L213	90	SEA ABB=ON	PLU=ON	(L209 OR L210 OR L211) AND L212
		D TRIAL 1-5		
L214	14371	SEA ABB=ON	PLU=ON	MATRIX? OR MATRIC?
L215	1	SEA ABB=ON	PLU=ON	L214 AND L213
		D TRIAL		
L216	2850	SEA ABB=ON	PLU=ON	SILICON?
L217	0	SEA ABB=ON	PLU=ON	L216 AND L213
L218	6737	SEA ABB=ON	PLU=ON	(PERMEAT? OR PENETRAT?) (1A) ENHANC?
L*** DEL	233	S L218 AND L212		
L219	1	SEA ABB=ON	PLU=ON	L218 AND L213
L220	1886	SEA ABB=ON	PLU=ON	ADHESIV?
L221	1	SEA ABB=ON	PLU=ON	L220 AND L213
		D TRIAL		
L222	0	SEA ABB=ON	PLU=ON	BANDAG? AND L213
L223	2	SEA ABB=ON	PLU=ON	PLASTER? AND L213
		D TRIAL 1-2		
L224	6731	SEA ABB=ON	PLU=ON	TRANSDERM?
L225	41	SEA ABB=ON	PLU=ON	L213 AND L224
		D TRIAL 1-3		
L226	1	SEA ABB=ON	PLU=ON	LAYER? AND L213
		D TRIAL		
		D KWIC		
		D SCA L213		
L227	1	SEA ABB=ON	PLU=ON	ESTER AND L213
		D TRIAL		
		D KWIC		
L228	4117	SEA ABB=ON	PLU=ON	CONTROL? (W) RELEAS?
L229	1	SEA ABB=ON	PLU=ON	L213 AND L228
		D TRIAL		
		D KWIC		
		D COST		

FILE 'STNGUIDE' ENTERED AT 14:21:43 ON 07 JUL 2006

FILE 'WPIX' ENTERED AT 14:31:38 ON 07 JUL 2006

FILE 'DRUGU' ENTERED AT 14:31:54 ON 07 JUL 2006

L230	1	SEA ABB=ON	PLU=ON	KLOKKERS K?/AU
L231	85	SEA ABB=ON	PLU=ON	KRAMER K?/AU
L232	95	SEA ABB=ON	PLU=ON	FISCHER W?/AU
L233	8	SEA ABB=ON	PLU=ON	SENDL A?/AU
L234	0	SEA ABB=ON	PLU=ON	SENDL LANG A?/AU
L235	0	SEA ABB=ON	PLU=ON	L230 AND (L231 OR L232 OR L233 OR L234)
L236	0	SEA ABB=ON	PLU=ON	L231 AND (L232 OR L233 OR L234)
L237	0	SEA ABB=ON	PLU=ON	L232 AND (L233 OR L234)
L238	0	SEA ABB=ON	PLU=ON	(L230 OR L231 OR L232 OR L233 OR L234) AND (L215 OR L217 OR L219 OR (L221 OR L222 OR L223))

FILE 'WPIX' ENTERED AT 14:34:05 ON 07 JUL 2006

L239	1259	SEA ABB=ON	PLU=ON	(L230 OR L231 OR L232 OR L233 OR L234)
L240	21	SEA ABB=ON	PLU=ON	(L235 OR L236 OR L237)
		D SCA		
L241	0	SEA ABB=ON	PLU=ON	L240 AND B/MC
L242	970	SEA ABB=ON	PLU=ON	B14-F02B1/MC
L243	882	SEA ABB=ON	PLU=ON	B12-F05A/MC
L244	16	SEA ABB=ON	PLU=ON	C14-F02B1/MC

L245 27 SEA ABB=ON PLU=ON C12-F05A/MC  
 L246 1852 SEA ABB=ON PLU=ON (L242 OR L243 OR L244 OR L245)  
 L247 3767 SEA ABB=ON PLU=ON B12-M02D/MC  
 L248 4457 SEA ABB=ON PLU=ON B12-M02F/MC  
 L249 278 SEA ABB=ON PLU=ON C12-M02F/MC  
 L250 209 SEA ABB=ON PLU=ON C12-M02D/MC  
 L251 7446 SEA ABB=ON PLU=ON (L247 OR L248 OR L249 OR L250)  
 L252 16 SEA ABB=ON PLU=ON L246 AND L251  
 D SCA  
 L253 2 SEA ABB=ON PLU=ON L240 AND L252

FILE 'STNGUIDE' ENTERED AT 14:41:42 ON 07 JUL 2006

FILE 'REGISTRY' ENTERED AT 14:43:28 ON 07 JUL 2006  
D IDE L2 1-15

FILE 'STNGUIDE' ENTERED AT 14:44:03 ON 07 JUL 2006

FILE 'HCAPLUS' ENTERED AT 14:48:07 ON 07 JUL 2006  
D QUE NOS L58

FILE 'MEDLINE' ENTERED AT 14:48:08 ON 07 JUL 2006  
D QUE NOS L88  
D QUE NOS L89

L254 2 SEA ABB=ON PLU=ON L88 OR L89

FILE 'EMBASE' ENTERED AT 14:48:11 ON 07 JUL 2006

D QUE NOS L98  
 D QUE NOS L99  
 D QUE NOS L100  
 D QUE NOS L97  
 D QUE NOS L101  
 D QUE NOS L197  
 D QUE NOS L198  
 D QUE NOS L199

L255 3 SEA ABB=ON PLU=ON (L97 OR L98 OR L99 OR L100 OR L101) OR  
(L197 OR L198 OR L199)

FILE 'BIOSIS' ENTERED AT 14:48:19 ON 07 JUL 2006  
D QUE NOS L208

FILE 'DRUGU' ENTERED AT 14:48:20 ON 07 JUL 2006  
D QUE NOS L238

FILE 'WPIX' ENTERED AT 14:48:22 ON 07 JUL 2006  
D QUE NOS L240  
D QUE NOS L253

L256 21 SEA ABB=ON PLU=ON L240 OR L253

FILE 'STNGUIDE' ENTERED AT 14:48:38 ON 07 JUL 2006

FILE 'HCAPLUS, MEDLINE, EMBASE, BIOSIS, WPIX' ENTERED AT 14:49:46 ON 07 JUL 2006

L257 43 DUP REM L58 L254 L255 L208 L238 L256 (18 DUPLICATES REMOVED)  
 ANSWERS '1-20' FROM FILE HCAPLUS  
 ANSWERS '21-22' FROM FILE MEDLINE  
 ANSWERS '23-25' FROM FILE EMBASE  
 ANSWERS '26-39' FROM FILE BIOSIS  
 ANSWERS '40-43' FROM FILE WPIX  
 D IBIB ABS HITIND HITSTR L257 1-20

D IALL L257 21-43

FILE 'STNGUIDE' ENTERED AT 14:51:46 ON 07 JUL 2006

FILE 'HCAPLUS' ENTERED AT 14:58:23 ON 07 JUL 2006

D QUE NOS L33

D QUE NOS L34

D QUE NOS L38

D QUE NOS L40

D QUE NOS L44

D QUE NOS L49

D QUE NOS L68

L258 28 SEA ABB=ON PLU=ON ((L33 OR L34) OR L38 OR L40 OR L44 OR L49  
OR L68) NOT L58

FILE 'MEDLINE' ENTERED AT 14:58:29 ON 07 JUL 2006

D QUE NOS L87

L259 11 SEA ABB=ON PLU=ON L87 NOT L254

FILE 'EMBASE' ENTERED AT 14:58:31 ON 07 JUL 2006

D QUE NOS L135

D QUE NOS L137

D QUE NOS L139

D QUE NOS L133

D QUE NOS L146

D QUE NOS L164

D QUE NOS L165

D QUE NOS L166

D QUE NOS L168

D QUE NOS L171

D QUE NOS L173

D QUE NOS L175

D QUE NOS L177

D QUE NOS L179

L260 15 SEA ABB=ON PLU=ON (L135 OR L137 OR L139 OR L133 OR L146 OR  
L164 OR L165 OR L166 OR L168 OR L171 OR L173 OR L175 OR L177  
OR L179) NOT L255

FILE 'BIOSIS' ENTERED AT 14:58:43 ON 07 JUL 2006

D QUE NOS L190

L261 1 SEA ABB=ON PLU=ON L190 NOT L208

FILE 'DRUGU' ENTERED AT 14:58:45 ON 07 JUL 2006

D QUE NOS L215

D QUE NOS L217

D QUE NOS L219

D QUE NOS L221

D QUE NOS L222

D QUE NOS L223

L262 3 SEA ABB=ON PLU=ON (L215 OR L217 OR L219 OR (L221 OR L222 OR  
L223)) NOT L238

FILE 'WPIX' ENTERED AT 14:58:53 ON 07 JUL 2006

D QUE NOS L252

L263 14 SEA ABB=ON PLU=ON L252 NOT L256

FILE 'STNGUIDE' ENTERED AT 14:59:08 ON 07 JUL 2006

FILE 'HCAPLUS, MEDLINE, EMBASE, BIOSIS, DRUGU, WPIX' ENTERED AT 15:00:01  
ON 07 JUL 2006

L264 63 DUP REM L258 L259 L260 L261 L262 L263 (9 DUPLICATES REMOVED)  
ANSWERS '1-28' FROM FILE HCAPLUS  
ANSWERS '29-39' FROM FILE MEDLINE  
ANSWERS '40-49' FROM FILE EMBASE  
ANSWER '50' FROM FILE BIOSIS  
ANSWERS '51-52' FROM FILE DRUGU  
ANSWERS '53-63' FROM FILE WPIX  
D IBIB ABS HITIND HITSTR L264 1-28  
D IALL L264 29-63

## FILE HOME

## FILE REGISTRY

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 6 JUL 2006 HIGHEST RN 890869-30-4  
DICTIONARY FILE UPDATES: 6 JUL 2006 HIGHEST RN 890869-30-4

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

## FILE HCAPLUS

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FILE COVERS 1907 - 7 Jul 2006 VOL 145 ISS 3  
FILE LAST UPDATED: 6 Jul 2006 (20060706/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

## FILE STNGUIDE

FILE CONTAINS CURRENT INFORMATION.

LAST RELOADED: Jun 30, 2006 (20060630/UP).

## FILE MEDLINE

FILE LAST UPDATED: 6 JUL 2006 (20060706/UP). FILE COVERS 1950 TO DATE.

On December 11, 2005, the 2006 MeSH terms were loaded.

The MEDLINE reload for 2006 is now (26 Feb.) available. For details on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>).  
See also:

<http://www.nlm.nih.gov/mesh/>  
[http://www.nlm.nih.gov/pubs/techbull/nd04/nd04\\_mesh.html](http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html)  
[http://www.nlm.nih.gov/pubs/techbull/nd05/nd05\\_med\\_data\\_changes.html](http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html)  
[http://www.nlm.nih.gov/pubs/techbull/nd05/nd05\\_2006\\_MeSH.html](http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html)

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

#### FILE EMBASE

FILE COVERS 1974 TO 7 Jul 2006 (20060707/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

EMBASE is now updated daily. SDI frequency remains weekly (default) and biweekly.

This file contains CAS Registry Numbers for easy and accurate substance identification.

#### FILE BIOSIS

FILE COVERS 1969 TO DATE.

CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNS) PRESENT  
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 5 July 2006 (20060705/ED)

#### FILE DRUGU

FILE LAST UPDATED: 3 JUL 2006 <20060703/UP>

>>> DERWENT DRUG FILE (SUBSCRIBER) <<<

>>> FILE COVERS 1983 TO DATE <<<

>>> THESAURUS AVAILABLE IN /CT <<<

#### FILE WPIX

FILE LAST UPDATED: 6 JUL 2006 <20060706/UP>

MOST RECENT DERWENT UPDATE: 200643 <200643/DW>

DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,  
PLEASE VISIT:  
[http://www.stn-international.de/training\\_center/patents/stn\\_guide.pdf](http://www.stn-international.de/training_center/patents/stn_guide.pdf) <

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES, SEE  
<http://scientific.thomson.com/support/patents/coverage/latestupdates/>

>>> PLEASE BE AWARE OF THE NEW IPC REFORM IN 2006, SEE

[http://www.stn-international.de/stndatabases/details/ipc\\_reform.html](http://www.stn-international.de/stndatabases/details/ipc_reform.html) and  
<http://scientific.thomson.com/media/scpdf/ipcrdwpi.pdf> <<<

>>> FOR FURTHER DETAILS ON THE FORTHCOMING DERWENT WORLD PATENTS  
INDEX ENHANCEMENTS PLEASE VISIT:

[http://www.stn-international.de/stndatabases/details/dwpi\\_r.html](http://www.stn-international.de/stndatabases/details/dwpi_r.html) <<<

=>

# DERWENT (WPix) CODES

Ghali 10/019121

07/07/2006

=> s b14-f02b1/mc  
B14-F02B1 "ANGIOTENSIN CONVERTING ENZYME INHIBITOR, ANGIOTENSIN ANTAGONISTS\*\*"  
L242 970 B14-F02B1/MC

=> s b12-f05a/mc  
B12-F05A "ANGIOTENSIN CONVERTING ENZYME INHIBITOR, RENIN INHIBITOR"  
L243 882 B12-F05A/MC

=> s c14-f02b1/mc  
C14-F02B1 "ANGIOTENSIN CONVERTING ENZYME INHIBITOR, ANGIOTENSIN ANTAGONISTS\*\*"  
L244 16 C14-F02B1/MC

=> s c12-f05a/mc  
C12-F05A "ANGIOTENSIN CONVERTING ENZYME INHIBITOR, RENIN INHIBITOR"  
L245 27 C12-F05A/MC

=> s b12-m02d/mc  
B12-M02D "ADHESIVE SHEET, STICKING PLASTER, BANDAGE"  
L247 3767 B12-M02D/MC

=> s b12-m02f/mc  
B12-M02F TRANSDERMAL  
L248 4457 B12-M02F/MC

=> s c12-m02f/mc  
C12-M02F TRANSDERMAL  
L249 278 C12-M02F/MC

=> s c12-m02d/mc  
C12-M02D "ADHESIVE SHEET, STICKING PLASTER, BANDAGE"  
L250 209 C12-M02D/MC

=> file registry  
FILE 'REGISTRY' ENTERED AT 14:43:28 ON 07 JUL 2006.  
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.  
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MATCH

STRUCTURE FILE UPDATES: 6 JUL 2006 HIGHEST RN 890869-30-4  
DICTIONARY FILE UPDATES: 6 JUL 2006 HIGHEST RN 890869-30-4

REGISTRY

New CAS Information Use Policies, enter HELP USAGETERMS for details. NUMBERS,

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

NAMES,

Please note that search-term pricing does apply when  
conducting SmartSELECT searches.

AND STRUCTURES

REGISTRY includes numerically searchable data for experimental and  
predicted properties as well as tags indicating availability of  
experimental property data in the original document. For information  
on property searching in REGISTRY, refer to:

TO

REFERENCES

<http://www.cas.org/ONLINE/UG/regprops.html>

=> d ide L2 1-15

L2 ANSWER 1 OF 15 REGISTRY COPYRIGHT 2006 ACS on STN  
RN 198292-69-2 REGISTRY  
ED Entered STN: 09 Dec 1997  
CN Duro-Tak 387-2353 (9CI) (CA INDEX NAME)  
ENTE An acrylate copolymer adhesive  
MF Unspecified  
CI MAN  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

13 REFERENCES IN FILE CA (1907 TO DATE)

13 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 2 OF 15 REGISTRY COPYRIGHT 2006 ACS on STN  
RN 103775-10-6 REGISTRY  
ED Entered STN: 18 Aug 1986  
CN 3-Isoquinolinecarboxylic acid, 2-[(2S)-2-[[1S]-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-6,7-dimethoxy-, (3S)-(9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

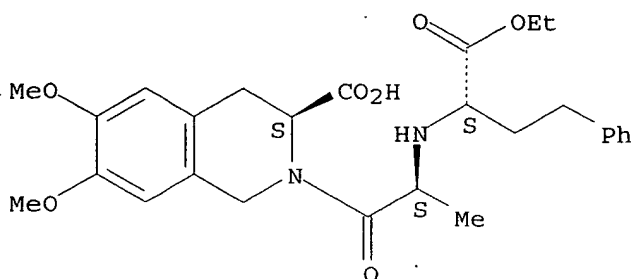
CN 3-Isoquinolinecarboxylic acid, 2-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-6,7-dimethoxy-, [3S-[2[R\*(R\*)],3R\*)]-

OTHER NAMES:

CN Moexipril  
CN RS 10085  
FS STEREOSEARCH  
DR 109715-88-0, 583815-17-2  
MF C27 H34 N2 O7  
CI COM  
SR CA

LC STN Files: ADISINSIGHT, ADISNEWS, BIOSIS, BIOTECHNO, CA, CAPLUS, CBNB, CHEMCATS, CIN, DDFU, DRUGU, EMBASE, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK\*, PHAR, PROMT, PROUSDDR, PS, RTECS\*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL  
 (\*File contains numerically searchable property data)  
 Other Sources: WHO

Absolute stereochemistry.

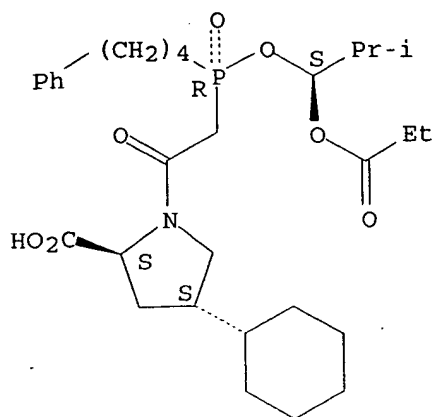


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

186 REFERENCES IN FILE CA (1907 TO DATE)  
 8 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 186 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 3 OF 15 REGISTRY COPYRIGHT 2006 ACS on STN  
 RN 98048-97-6 REGISTRY  
 ED Entered STN: 16 Sep 1985  
 CN L-Proline, 4-cyclohexyl-1-[[[2-methyl-1-(1-oxopropoxy)propoxy] (4-phenylbutyl)phosphinyl]acetyl]-, (4S)- (9CI) (CA INDEX NAME)  
 OTHER CA INDEX NAMES:  
 CN L-Proline, 4-cyclohexyl-1-[[[2-methyl-1-(1-oxopropoxy)propoxy] (4-phenylbutyl)phosphinyl]acetyl]-, [1[S\*(R\*)], 2 $\alpha$ , 4 $\beta$ ]-  
 OTHER NAMES:  
 CN Fosenopril  
 CN Fosinopril  
 FS STEREOSEARCH  
 DR 128947-97-7, 97825-24-6  
 MF C30 H46 N O7 P  
 CI COM  
 SR CA  
 LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, DDFU, DRUGU, EMBASE, IFICDB, IFIUDB, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK\*, PATDPASPC, PHAR, PROMT, PROUSDDR, PS, RTECS\*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL  
 (\*File contains numerically searchable property data)  
 Other Sources: WHO

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

574 REFERENCES IN FILE CA (1907 TO DATE)  
 17 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 574 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 4 OF 15 REGISTRY COPYRIGHT 2006 ACS on STN  
 RN 89371-37-9 REGISTRY  
 ED Entered STN: 16 Nov 1984  
 CN 4-Imidazolidinecarboxylic acid, 3-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1-methyl-2-oxo-, (4S)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 4-Imidazolidinecarboxylic acid, 3-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1-methyl-2-oxo-, [4S-[3[R\*(R\*)],4R\*]]-

OTHER NAMES:

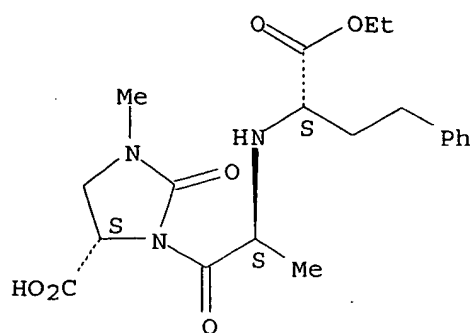
CN Imidapril  
 FS STEREOSEARCH  
 MF C20 H27 N3 O6  
 CI COM

LC STN Files: ADISINSIGHT, ADISNEWS, ANABSTR, BEILSTEIN\*, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CIN, DDFU, DRUGU, EMBASE, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MRCK\*, PATDPASPC, PHAR, PROMT, PROUSDDR, PS, RTECS\*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL

(\*File contains numerically searchable property data)

Other Sources: WHO

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

286 REFERENCES IN FILE CA (1907 TO DATE)

6 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

287 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 5 OF 15 REGISTRY COPYRIGHT 2006 ACS on STN

RN 88768-40-5 REGISTRY

ED Entered STN: 16 Nov 1984

CN 6H-Pyridazino[1,2-a][1,2]diazepine-1-carboxylic acid, 9-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]octahydro-10-oxo-, (1S,9S)- (9CI)  
(CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 6H-Pyridazino[1,2-a][1,2]diazepine-1-carboxylic acid, 9-[[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]octahydro-10-oxo-, [1S-[1 $\alpha$ ,9 $\alpha$ (R\*)]]-]

OTHER NAMES:

CN Cilazapril

CN Ro 31-2848

CN Vascace

CN Yipingshu

FS STEREOSEARCH

DR 856439-81-1

MF C22 H31 N3 O5

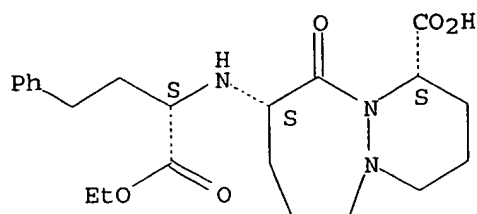
CI COM

LC STN Files: ADISNEWS, ANABSTR, BEILSTEIN\*, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, DDFU, DRUGU, EMBASE, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK\*, PATDPASPC, PHAR, PROMT, PROUSDDR, PS, RTECS\*, SCISEARCH, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL

(\*File contains numerically searchable property data)

Other Sources: WHO

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

543 REFERENCES IN FILE CA (1907 TO DATE)  
 11 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 544 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 6 OF 15 REGISTRY COPYRIGHT 2006 ACS on STN  
 RN 87679-71-8 REGISTRY  
 ED Entered STN: 16 Nov 1984  
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-carboxy-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aR,7aS)-(9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 1H-Indole-2-carboxylic acid, 1-[2-[(1-carboxy-3-phenylpropyl)amino]-1-oxopropyl]octahydro-, [2S-[1[R\*(R\*)],2 $\alpha$ ,3 $\alpha$ ,7 $\alpha$ ]]-

OTHER NAMES:

CN RU 44403

CN Trandolaprilat

CN Trandolaprilate

FS STEREOSEARCH

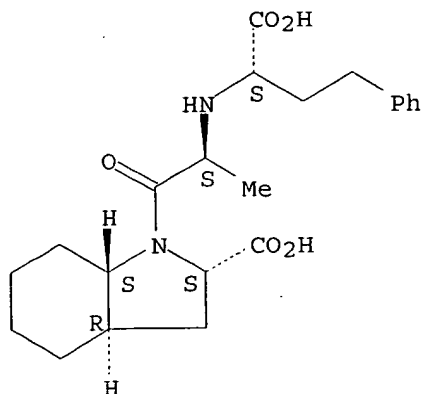
DR 114612-74-7

MF C22 H30 N2 O5

LC STN Files: ADISNEWS, BEILSTEIN\*, BIOSIS, CA, CAPLUS, CHEMCATS, DDFU, DRUGU, IPA, MRCK\*, PHAR, PROUSDDR, TOXCENTER, USAN, USPATFULL  
 (\*File contains numerically searchable property data)

Other Sources: WHO

Absolute stereochemistry.



## \*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

59 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

59 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 7 OF 15 REGISTRY COPYRIGHT 2006 ACS on STN

RN 87679-37-6 REGISTRY

ED Entered STN: 16 Nov 1984

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aR,7aS)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, [2S-[1[R\*(R\*)],2 $\alpha$ ,3 $\alpha$ ,7 $\alpha$ ]]-

OTHER NAMES:

CN Gopten

CN Mavick

CN Odrik

CN RU 44570

CN Trandolapril

FS STEREOSEARCH

MF C24 H34 N2 O5

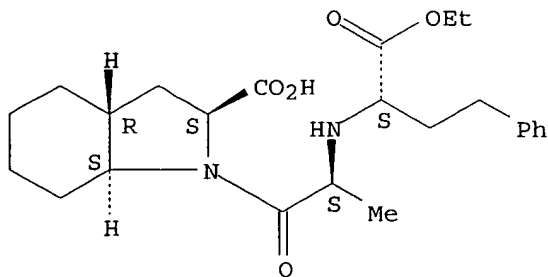
CI COM

LC STN Files: ADISINSIGHT, ADISNEWS, ANABSTR, BEILSTEIN\*, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, DDFU, DRUGU, EMBASE, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK\*, PATDPASPC, PROMT, PROUSDDR, PS, RTECS\*, SCISEARCH, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL

(\*File contains numerically searchable property data)

Other Sources: WHO

Absolute stereochemistry. Rotation (-).



## \*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

536 REFERENCES IN FILE CA (1907 TO DATE)

15 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

537 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 8 OF 15 REGISTRY COPYRIGHT 2006 ACS on STN

RN 87333-19-5 REGISTRY

ED Entered STN: 16 Nov 1984

CN Cyclopenta[b]pyrrole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-

(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-,  
(2S,3aS,6aS)-(9CI) (CA INDEX NAME)

## OTHER CA INDEX NAMES:

CN Cyclopenta[b]pyrrole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, [2S-  
[1[R\*(R\*)],2 $\alpha$ ,3a $\beta$ ,6a $\beta$ ]]-

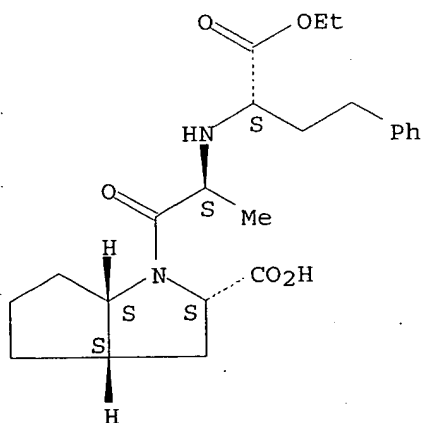
## OTHER NAMES:

CN Altace  
CN Cardace  
CN Delix  
CN HOE 498  
CN Pramace  
CN Quark  
CN Ramace  
CN Ramipril  
CN Triatec  
CN Tritace  
CN Unipril  
CN Vesdil  
FS STEREOSEARCH  
DR 126613-39-6  
MF C23 H32 N2 O5  
CI COM

LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN\*, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, CSCHM, CSNB, DDFU, DRUGU, EMBASE, IMSCOSEARCH, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK\*, MSDS-OHS, PATDPASPC, PHAR, PROMT, PROUSDDR, PS, RTECS\*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL  
(\*File contains numerically searchable property data)

Other Sources: WHO

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1137 REFERENCES IN FILE CA (1907 TO DATE)  
22 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
1141 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 9 OF 15 REGISTRY COPYRIGHT 2006 ACS on STN  
RN 87269-97-4 REGISTRY  
ED Entered STN: 16 Nov 1984

OTHER CA INDEX NAMES:

OTHER NAMES :

CN Ramipril diacid

FS STEREOSEARCH

CI	COM
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100	100

Other Sources: WHO

The chemical structure shows a pentathiane ring (a five-membered ring with three sulfur atoms and two carbon atoms). The ring is substituted with a carboxylic acid group ( $\text{CO}_2\text{H}$ ) at position 1, a methyl group ( $\text{Me}$ ) at position 2, and a 3-phenylpropanesulfonamido group ( $\text{NH-S-CH}_2\text{CH}_2\text{Ph}$ ) at position 3. The stereochemistry is indicated by wedges and dashes: the carboxylic acid group at position 1 is dashed, the methyl group at position 2 is wedged, and the 3-phenylpropanesulfonamido group at position 3 is wedged. The ring carbons are also substituted with hydrogen atoms: the carbon at position 1 has a wedged hydrogen, and the carbon at position 2 has a dashed hydrogen.

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

3 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

230 REFERENCES IN FILE CAPLUS (1907 TO DATE)

RN 86541-75-5 REGISTRY

CN 1H-1-Benzazepine-1-acetic acid, 3-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-2,3,4,5-tetrahydro-2-oxo-, (3S)- (9CI) (CA INDEX NAME)

CN 1H-1-Benzazepine-1-acetic acid, 3-[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-2,3,4,5-tetrahydro-2-oxo-, [S-(R\*,R\*)]-

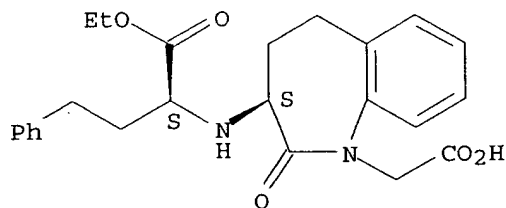
CN Benapril

CN	Benazepril
----	------------

CN Briem

CN Cibacen  
 CN Cibacen WS  
 CN Cibacene  
 FS STEREOSEARCH  
 DR 116764-54-6  
 MF C24 H28 N2 O5  
 CI COM  
 LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN\*, BIOSIS, BIOTECHNO,  
 CA, CAPLUS, CBNB, CHEMCATS, CIN, DDFU, DRUGU, EMBASE, HSDB\*,  
 IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK\*, PATDPASPC,  
 PHAR, PROMT, PROUSDDR, PS, RTECS\*, SYNTHLINE, TOXCENTER, USAN, USPAT2,  
 USPATFULL, VETU  
 (\*File contains numerically searchable property data)  
 Other Sources: WHO

Absolute stereochemistry.

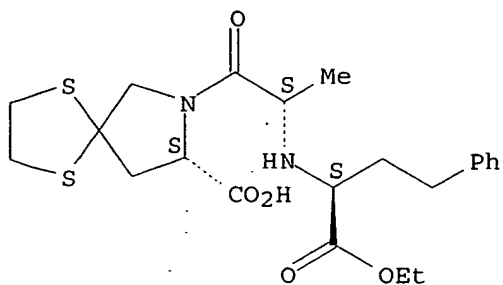


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

570 REFERENCES IN FILE CA (1907 TO DATE)  
 14 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 572 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 11 OF 15 REGISTRY COPYRIGHT 2006 ACS on STN  
 RN 83647-97-6 REGISTRY  
 ED Entered STN: 16 Nov 1984  
 CN 1,4-Dithia-7-azaspiro[4.4]nonane-8-carboxylic acid, 7-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-, (8S)- (9CI) (CA INDEX NAME)  
 OTHER CA INDEX NAMES:  
 CN 1,4-Dithia-7-azaspiro[4.4]nonane-8-carboxylic acid, 7-[2-[[[1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-, [8S-[7[R\*(R)],8R\*]]-  
 OTHER NAMES:  
 CN Sch 33844  
 CN Spirapril  
 FS STEREOSEARCH  
 MF C22 H30 N2 O5 S2  
 CI COM  
 LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN\*, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CIN, DDFU, DRUGU, EMBASE, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK\*, PHAR, PROMT, PROUSDDR, PS, RTECS\*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL  
 (\*File contains numerically searchable property data)  
 Other Sources: WHO

Absolute stereochemistry. Rotation (-).



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

189 REFERENCES IN FILE CA (1907 TO DATE)

8 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

189 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 12 OF 15 REGISTRY COPYRIGHT 2006 ACS on STN

RN 82834-16-0 REGISTRY

ED Entered STN: 16 Nov 1984

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-(9CI)  
(CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 1H-Indole-2-carboxylic acid, 1-[2-[[1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, [2S-[1[R\*(R\*)],2 $\alpha$ ,3 $\alpha\beta$ ,7 $\alpha\beta$ ]]-

OTHER NAMES:

CN McN-A 2833

CN Perindopril

CN S 9490

FS STEREOSEARCH

DR 99149-83-4

MF C19 H32 N2 O5

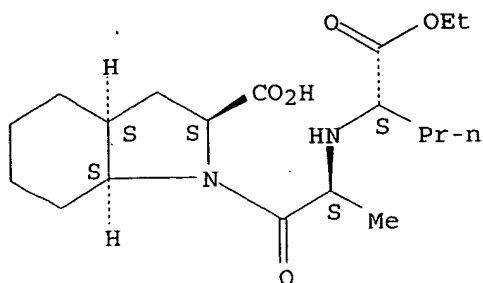
CI COM

LC STN Files: ADISNEWS, ANABSTR, BEILSTEIN\*, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, DDFU, DRUGU, EMBASE, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK\*, PATDPASPC, PHAR, PROMT, PROUSDDR, PS, RTECS\*, SCISEARCH, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL

(\*File contains numerically searchable property data)

Other Sources: WHO

Absolute stereochemistry. Rotation (-).



**\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\***

896 REFERENCES IN FILE CA (1907 TO DATE)  
 18 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 897 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 13 OF 15 REGISTRY COPYRIGHT 2006 ACS on STN  
 RN 9015-82-1 REGISTRY  
 ED Entered STN: 16 Nov 1984  
 CN Carboxypeptidase, dipeptidyl, A (9CI) (CA INDEX NAME)  
 OTHER NAMES:

CN ACE  
 CN ACE (enzyme)  
 CN Angiotensin I-converting enzyme  
 CN Angiotensin-1 converting enzyme  
 CN Angiotensin-converting enzyme  
 CN Angiotensin-converting enzyme I  
 CN Angiotension-converting enzyme  
 CN Carboxycathepsin  
 CN Carboxypeptidase Zace2  
 CN Dipeptidyl carboxypeptidase  
 CN Dipeptidyl carboxypeptidase A  
 CN Dipeptidyl carboxypeptidase I  
 CN Dipeptidyl serine carboxypeptidase  
 CN E.C. 3.4.15.1  
 CN Endothelial cell peptidyl dipeptidase  
 CN Kininase II  
 CN Peptidase P  
 CN Peptidyl dipeptidase  
 CN Peptidyl dipeptidase A  
 CN Peptidyl dipeptidase-4  
 CN Peptidyldipeptide hydrolase A  
 CN Vasopeptidase  
 CN Zinc metallopeptidase Zace1  
 MF Unspecified  
 CI MAN  
 LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOSIS, BIOTECHNO, CA, CABA,  
 CAPLUS, CASREACT, CBNB, CHEMCATS, CIN, CSCHEM, CSNB, EMBASE, IFICDB,  
 IFIPAT, IFIUDB, IPA, PROMT, TOXCENTER, USPAT2, USPATFULL

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

**\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\***

16418 REFERENCES IN FILE CA (1907 TO DATE)  
 65 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

## 16437 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 14 OF 15 REGISTRY COPYRIGHT 2006 ACS on STN  
RN 7631-86-9 REGISTRY  
ED Entered STN: 16 Nov 1984  
CN Silica (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

## OTHER NAMES:

CN 1135MP  
CN 1165MP  
CN 165MPJ  
CN 175GR  
CN 255S  
CN 300CF  
CN 30R50  
CN 30R7  
CN 3K  
CN 3KS  
CN 400G  
CN 400WQ  
CN 5085HSD30  
CN 5085SD30  
CN 5X  
CN 7000GR  
CN 937L  
CN 940UP  
CN 955W  
CN 980H  
CN A 150  
CN A 175  
CN A 200  
CN A 300  
CN A 380  
CN Acematt HK 400  
CN Acematt TS 100  
CN Acrifix 122  
CN Acticel  
CN Adelite 20N  
CN Adelite 30  
CN Adelite A  
CN Adelite AD 321  
CN Adelite AT  
CN Adelite AT 20  
CN Adelite AT 2045  
CN Adelite AT 20A  
CN Adelite AT 20N  
CN Adelite AT 20Q  
CN Adelite AT 20S  
CN Adelite AT 30  
CN Adelite AT 30A  
CN Adelite AT 30B  
CN Adelite AT 30S  
CN Adelite AT 40  
CN Adelite AT 50  
CN Adelite BT 55  
CN Adelite BT 59  
CN Adelite CT 100  
CN Adelite CT 300

ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for  
DISPLAY

FS 3D CONCORD

DR 11139-72-3, 11139-73-4, 12125-13-2, 12737-36-9, 12753-63-8, 12765-74-1,  
12774-28-6, 9049-77-8, 1340-09-6, 172306-09-1, 173299-41-7, 127689-16-1,  
127831-27-0, 126879-14-9, 126879-30-9, 126879-49-0, 53468-64-7,  
125623-17-8, 56645-27-3, 56731-06-7, 122985-48-2, 55599-33-2, 60572-11-4,  
62655-73-6, 97343-62-9, 97709-14-3, 98226-40-5, 98253-25-9, 67167-16-2,  
113384-41-1, 50813-13-3, 50926-93-7, 50935-83-6, 51542-57-5, 51542-58-6,  
61673-46-9, 108727-71-5, 136303-13-4, 136881-80-6, 37220-24-9, 37241-25-1,  
37334-65-9, 37340-45-7, 37380-93-1, 138860-82-9, 139074-73-0, 137263-03-7,  
145537-54-8, 145686-91-5, 145808-77-1, 70536-23-1, 70536-61-7, 70563-35-8,  
78207-17-7, 146585-72-0, 152206-35-4, 152787-33-2, 155552-25-3,  
155575-05-6, 83589-56-4, 83652-92-0, 149779-02-2, 87501-59-5, 89493-21-0,  
39336-66-8, 39372-58-2, 39409-25-1, 39443-40-8, 39456-81-0, 52350-43-3,  
107497-59-6, 179046-03-8, 184654-53-3, 185461-90-9, 188357-77-9,  
191289-29-9, 203526-86-7, 206770-31-2, 207868-97-1, 217643-58-8,  
231629-15-5, 247900-77-2, 250579-70-5, 250579-78-3, 264907-28-0,  
330152-64-2, 341028-71-5, 368432-40-0, 402828-37-9, 402828-39-1,  
402828-40-4

MF 02 Si

CI COM

SR CA

LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BIOSIS, BIOTECHNO,  
CA, CABA, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMINFORMRX,  
CHEMLIST, CHEMSAFE, CIN, CSCHEM, CSNB, DDFU, DETHERM\*, DRUGU, EMBASE,  
ENCOMPLIT, ENCOMPLIT2, ENCOMPPAT, ENCOMPPAT2, GMELIN\*, HSDB\*, IFICDB,  
IFIPAT, IFIUDB, IPA, MEDLINE, MRCK\*, MSDS-OHS, NAPRALERT, PIRA, PROMT,  
RTECS\*, TOXCENTER, TULSA, ULIDAT, USAN, USPAT2, USPATFULL, VETU, VTB  
(\*File contains numerically searchable property data)  
Other Sources: DSL\*\*, EINECS\*\*, TSCA\*\*  
(\*\*Enter CHEMLIST File for up-to-date regulatory information)

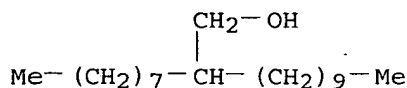
O=Si=O

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

355324 REFERENCES IN FILE CA (1907 TO DATE)  
7458 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
355890 REFERENCES IN FILE CAPLUS (1907 TO DATE)  
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L2 ANSWER 15 OF 15 REGISTRY COPYRIGHT 2006 ACS on STN  
RN 5333-42-6 REGISTRY  
ED Entered STN: 16 Nov 1984  
CN 1-Dodecanol, 2-octyl- (7CI, 8CI, 9CI) (CA INDEX NAME)  
OTHER NAMES:  
CN 2-Octyl-1-dodecanol  
CN 2-Octyldodecanol  
CN 2-Octyldodecyl alcohol  
CN Eutanol G  
CN Exxal 20  
CN Isofol 20  
CN Kalcohl 200G  
CN Kalcohl 200GD  
CN NSC 2405  
CN Rilanit G 20  
FS 3D CONCORD  
DR 8039-11-0, 125200-13-7, 123897-20-1, 179606-99-6  
MF C20 H42 O

CI COM  
 LC STN Files: BEILSTEIN\*, BIOSIS, BIOTECHNO, CA, CAOLD, CAPLUS, CASREACT,  
 CHEMCATS, CHEMLIST, CIN, CSCHEM, DETHERM\*, EMBASE, IFICDB, IFIPAT,  
 IFIUIDB, IPA, MEDLINE, MSDS-OHS, RTECS\*, TOXCENTER, USPAT2, USPATFULL  
 (\*File contains numerically searchable property data)  
 Other Sources: DSL\*\*, EINECS\*\*, TSCA\*\*  
 (\*\*Enter CHEMLIST File for up-to-date regulatory information)



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

546 REFERENCES IN FILE CA (1907 TO DATE)  
 49 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 550 REFERENCES IN FILE CAPLUS (1907 TO DATE)  
 1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=> => file hcaplus

FILE 'HCAPLUS' ENTERED AT 14:48:07 ON 07 JUL 2006

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

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AUTHOR SEARCH

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FILE COVERS 1907 - 7 Jul 2006 VOL 145 ISS 3

FILE LAST UPDATED: 6 Jul 2006 (20060706/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

=> d que nos L58

L50	26	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	KLOKKERS K?/AU
L51	897	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	KRAMER K?/AU
L52	2531	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	FISCHER W?/AU
L53	11	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	SENDL A?/AU
L54	6	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	SENDL LANG A?/AU
L55	16	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L50 AND ((L51 OR L52 OR L53 OR L54))
L56	1	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L51 AND (L52 OR L53 OR L54)
L57	6	SEA	FILE=HCAPLUS	ABB=ON	PLU=ON	L52 AND (L53 OR L54)

L58 20 SEA FILE=HCAPLUS ABB=ON PLU=ON (L55 OR L56 OR L57)

=> file medline

FILE 'MEDLINE' ENTERED AT 14:48:08 ON 07 JUL 2006

FILE LAST UPDATED: 6 JUL 2006 (20060706/UP). FILE COVERS 1950 TO DATE.

On December 11, 2005, the 2006 MeSH terms were loaded.

The MEDLINE reload for 2006 is now (26 Feb.) available. For details on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>). See also:

<http://www.nlm.nih.gov/mesh/>  
[http://www.nlm.nih.gov/pubs/techbull/nd04/nd04\\_mesh.html](http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html)  
[http://www.nlm.nih.gov/pubs/techbull/nd05/nd05\\_med\\_data\\_changes.html](http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html)  
[http://www.nlm.nih.gov/pubs/techbull/nd05/nd05\\_2006\\_MeSH.html](http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html)

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d que nos L88

L12	3	SEA FILE=REGISTRY ABB=ON	PLU=ON	IMIDAPRIL?/CN
L13	4	SEA FILE=REGISTRY ABB=ON	PLU=ON	FOSINOPRIL?/CN
L14	3	SEA FILE=REGISTRY ABB=ON	PLU=ON	MOEXIPRIL?/CN
L15	8	SEA FILE=REGISTRY ABB=ON	PLU=ON	PERINDOPRIL?/CN
L16	5	SEA FILE=REGISTRY ABB=ON	PLU=ON	RAMIPRIL?/CN
L17	3	SEA FILE=REGISTRY ABB=ON	PLU=ON	SPIRAPRIL?/CN
L18	6	SEA FILE=REGISTRY ABB=ON	PLU=ON	CILAZAPRIL?/CN
L19	5	SEA FILE=REGISTRY ABB=ON	PLU=ON	BENAZEPRIL?/CN
L20	4	SEA FILE=REGISTRY ABB=ON	PLU=ON	TRANDOLAPRIL?/CN
L21	41	SEA FILE=REGISTRY ABB=ON	PLU=ON	(L12 OR L13 OR L14 OR L15 OR L16 OR L17 OR L18 OR L19 OR L20)
L69	0	SEA FILE=MEDLINE ABB=ON	PLU=ON	KLOKKERS K?/AU
L70	556	SEA FILE=MEDLINE ABB=ON	PLU=ON	KRAMER K?/AU
L71	931	SEA FILE=MEDLINE ABB=ON	PLU=ON	FISCHER W?/AU
L72	7	SEA FILE=MEDLINE ABB=ON	PLU=ON	SENDL A?/AU
L74	30261	SEA FILE=MEDLINE ABB=ON	PLU=ON	ANGIOTENSIN-CONVERTING ENZYME INHIBITORS+NT/CT
L75	4016	SEA FILE=MEDLINE ABB=ON	PLU=ON	L21
L76	30376	SEA FILE=MEDLINE ABB=ON	PLU=ON	(L74 OR L75)
L88	1	SEA FILE=MEDLINE ABB=ON	PLU=ON	(L69 OR L70 OR L71 OR L72) AND L76

=> d que nos L89

L69	0	SEA FILE=MEDLINE ABB=ON	PLU=ON	KLOKKERS K?/AU
L70	556	SEA FILE=MEDLINE ABB=ON	PLU=ON	KRAMER K?/AU
L71	931	SEA FILE=MEDLINE ABB=ON	PLU=ON	FISCHER W?/AU
L72	7	SEA FILE=MEDLINE ABB=ON	PLU=ON	SENDL A?/AU
L77	8710	SEA FILE=MEDLINE ABB=ON	PLU=ON	ADMINISTRATION, CUTANEOUS/CT

L89           1 SEA FILE=MEDLINE ABB=ON   PLU=ON   (L69 OR L70 OR L71 OR L72)  
              AND L77

=> s L88 or L89

L254           2 L88 OR L89

=> file embase

FILE 'EMBASE' ENTERED AT 14:48:11 ON 07 JUL 2006  
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FILE COVERS 1974 TO 7 Jul 2006 (20060707/ED)

EMBASE has been reloaded.. Enter HELP RLOAD for details.

EMBASE is now updated daily. SDI frequency remains weekly (default)  
and biweekly.

This file contains CAS Registry Numbers for easy and accurate  
substance identification.

=> d que nos L98

L93           2 SEA FILE=EMBASE ABB=ON   PLU=ON   KLOKKERS K?/AU  
L94           386 SEA FILE=EMBASE ABB=ON   PLU=ON   KRAMER K?/AU  
L95           664 SEA FILE=EMBASE ABB=ON   PLU=ON   FISCHER W?/AU  
L96           11 SEA FILE=EMBASE ABB=ON   PLU=ON   SENDL A?/AU  
L98           0 SEA FILE=EMBASE ABB=ON   PLU=ON   L93 AND (L94 OR L95 OR L96)

=> d que nos L99

L94           386 SEA FILE=EMBASE ABB=ON   PLU=ON   KRAMER K?/AU  
L95           664 SEA FILE=EMBASE ABB=ON   PLU=ON   FISCHER W?/AU  
L96           11 SEA FILE=EMBASE ABB=ON   PLU=ON   SENDL A?/AU  
L99           0 SEA FILE=EMBASE ABB=ON   PLU=ON   L94 AND (L95 OR L96)

=> d que nos L100

L95           664 SEA FILE=EMBASE ABB=ON   PLU=ON   FISCHER W?/AU  
L96           11 SEA FILE=EMBASE ABB=ON   PLU=ON   SENDL A?/AU  
L100           0 SEA FILE=EMBASE ABB=ON   PLU=ON   L95 AND L96

=> d que nos L97

L97           0 SEA FILE=EMBASE ABB=ON   PLU=ON   SENDL LANG A?/AU

=> d que nos L101

L92           69828 SEA FILE=EMBASE ABB=ON   PLU=ON   DIPEPTIDYL CARBOXYPEPTIDASE  
              INHIBITOR+NT/CT  
L93           2 SEA FILE=EMBASE ABB=ON   PLU=ON   KLOKKERS K?/AU  
L94           386 SEA FILE=EMBASE ABB=ON   PLU=ON   KRAMER K?/AU  
L95           664 SEA FILE=EMBASE ABB=ON   PLU=ON   FISCHER W?/AU  
L96           11 SEA FILE=EMBASE ABB=ON   PLU=ON   SENDL A?/AU

L97 0 SEA FILE=EMBASE ABB=ON PLU=ON SENDL LANG A?/AU  
 L101 1 SEA FILE=EMBASE ABB=ON PLU=ON L92 AND (L93 OR L94 OR L95 OR  
 L96 OR L97)

=> d que nos L197

L12 3 SEA FILE=REGISTRY ABB=ON PLU=ON IMIDAPRIL?/CN  
 L13 4 SEA FILE=REGISTRY ABB=ON PLU=ON FOSINOPRIL?/CN  
 L14 3 SEA FILE=REGISTRY ABB=ON PLU=ON MOEXIPRIL?/CN  
 L15 8 SEA FILE=REGISTRY ABB=ON PLU=ON PERINDOPRIL?/CN  
 L16 5 SEA FILE=REGISTRY ABB=ON PLU=ON RAMIPRIL?/CN  
 L17 3 SEA FILE=REGISTRY ABB=ON PLU=ON SPIRAPRIL?/CN  
 L18 6 SEA FILE=REGISTRY ABB=ON PLU=ON CILAZAPRIL?/CN  
 L19 5 SEA FILE=REGISTRY ABB=ON PLU=ON BENAZEPRIL?/CN  
 L20 4 SEA FILE=REGISTRY ABB=ON PLU=ON TRANDOLAPRIL?/CN  
 L21 41 SEA FILE=REGISTRY ABB=ON PLU=ON (L12 OR L13 OR L14 OR L15 OR  
 L16 OR L17 OR L18 OR L19 OR L20)  
 L92 69828 SEA FILE=EMBASE ABB=ON PLU=ON DIPEPTIDYL CARBOXYPEPTIDASE  
 INHIBITOR+NT/CT  
 L93 2 SEA FILE=EMBASE ABB=ON PLU=ON KLOKKERS K?/AU  
 L94 386 SEA FILE=EMBASE ABB=ON PLU=ON KRAMER K?/AU  
 L95 664 SEA FILE=EMBASE ABB=ON PLU=ON FISCHER W?/AU  
 L96 11 SEA FILE=EMBASE ABB=ON PLU=ON SENDL A?/AU  
 L97 0 SEA FILE=EMBASE ABB=ON PLU=ON SENDL LANG A?/AU  
 L102 11458 SEA FILE=EMBASE ABB=ON PLU=ON L21  
 L123 427 SEA FILE=EMBASE ABB=ON PLU=ON RAMIPRILAT  
 L124 391 SEA FILE=EMBASE ABB=ON PLU=ON IMIDAPRIL##  
 L125 1748 SEA FILE=EMBASE ABB=ON PLU=ON FOSIN!PRIL##  
 L126 253 SEA FILE=EMBASE ABB=ON PLU=ON MOEX!PRIL##  
 L127 3220 SEA FILE=EMBASE ABB=ON PLU=ON PERIND!PRIL##  
 L128 5309 SEA FILE=EMBASE ABB=ON PLU=ON RAM!PRIL##  
 L129 281 SEA FILE=EMBASE ABB=ON PLU=ON SPIR!PRIL##  
 L130 1461 SEA FILE=EMBASE ABB=ON PLU=ON CILAZ!PRIL##  
 L131 1496 SEA FILE=EMBASE ABB=ON PLU=ON BENAZ!PRIL##  
 L132 1723 SEA FILE=EMBASE ABB=ON PLU=ON TRAND!L!PRIL##  
 L140 69918 SEA FILE=EMBASE ABB=ON PLU=ON L92 OR L102 OR (L123 OR L124  
 OR L125 OR L126 OR L127 OR L128 OR L129 OR L130 OR L131 OR  
 L132)  
 L197 1 SEA FILE=EMBASE ABB=ON PLU=ON (L93 OR L94 OR L95 OR L96 OR  
 L97) AND L140

=> d que nos L198

L93 2 SEA FILE=EMBASE ABB=ON PLU=ON KLOKKERS K?/AU  
 L94 386 SEA FILE=EMBASE ABB=ON PLU=ON KRAMER K?/AU  
 L95 664 SEA FILE=EMBASE ABB=ON PLU=ON FISCHER W?/AU  
 L96 11 SEA FILE=EMBASE ABB=ON PLU=ON SENDL A?/AU  
 L97 0 SEA FILE=EMBASE ABB=ON PLU=ON SENDL LANG A?/AU  
 L162 11038 SEA FILE=EMBASE ABB=ON PLU=ON TRANSDERMAL DRUG ADMINISTRATION  
 /CT  
 L198 2 SEA FILE=EMBASE ABB=ON PLU=ON (L93 OR L94 OR L95 OR L96 OR  
 L97) AND L162

=>.d que nos L199

L92 69828 SEA FILE=EMBASE ABB=ON PLU=ON DIPEPTIDYL CARBOXYPEPTIDASE  
 INHIBITOR+NT/CT

```

L93      2 SEA FILE=EMBASE ABB=ON PLU=ON KLOKKERS K?/AU
L94      386 SEA FILE=EMBASE ABB=ON PLU=ON KRAMER K?/AU
L95      664 SEA FILE=EMBASE ABB=ON PLU=ON FISCHER W?/AU
L96      11 SEA FILE=EMBASE ABB=ON PLU=ON SENDL A?/AU
L97      0 SEA FILE=EMBASE ABB=ON PLU=ON SENDL LANG A?/AU
L199     1 SEA FILE=EMBASE ABB=ON PLU=ON (L93 OR L94 OR L95 OR L96 OR
      L97) AND L92

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=> s L97-L101 or L197-L199

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L255     3 (L97 OR L98 OR L99 OR L100 OR L101) OR (L197 OR L198 OR L199)

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=> file biosis

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FILE COVERS 1969 TO DATE.  
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNS) PRESENT  
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 5 July 2006 (20060705/ED)

=> d que nos L208

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L200     15 SEA FILE=BIOSIS ABB=ON PLU=ON KLOKKERS K?/AU
L201     812 SEA FILE=BIOSIS ABB=ON PLU=ON KRAMER K?/AU
L202     881 SEA FILE=BIOSIS ABB=ON PLU=ON FISCHER W?/AU
L203      13 SEA FILE=BIOSIS ABB=ON PLU=ON SENDL A?/AU
L204       5 SEA FILE=BIOSIS ABB=ON PLU=ON SENDL LANG A?/AU
L205     12 SEA FILE=BIOSIS ABB=ON PLU=ON L200 AND (L201 OR L202 OR L203
      OR L204)
L206      0 SEA FILE=BIOSIS ABB=ON PLU=ON L201 AND (L202 OR L203 OR
      L204)
L207      5 SEA FILE=BIOSIS ABB=ON PLU=ON L202 AND (L203 OR L204)
L208     15 SEA FILE=BIOSIS ABB=ON PLU=ON (L205 OR L206 OR L207)

```

=> file drugu

FILE 'DRUGU' ENTERED AT 14:48:20 ON 07 JUL 2006  
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FILE LAST UPDATED: 3 JUL 2006      <20060703/UP>
>>> DERWENT DRUG FILE (SUBSCRIBER) <<<

>>> FILE COVERS 1983 TO DATE <<<
>>> THESAURUS AVAILABLE IN /CT <<<

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=> d que nos L238

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L124     391 SEA FILE=EMBASE ABB=ON PLU=ON IMIDAPRIL##
L125    1748 SEA FILE=EMBASE ABB=ON PLU=ON FOSIN!PRIL##
L126     253 SEA FILE=EMBASE ABB=ON PLU=ON MOEX!PRIL##
L127    3220 SEA FILE=EMBASE ABB=ON PLU=ON PERIND!PRIL##
L128    5309 SEA FILE=EMBASE ABB=ON PLU=ON RAM!PRIL##
L129     281 SEA FILE=EMBASE ABB=ON PLU=ON SPIR!PRIL##

```

L130 1461 SEA FILE=EMBASE ABB=ON PLU=ON CILAZ!PRIL##  
 L131 1496 SEA FILE=EMBASE ABB=ON PLU=ON BENAZ!PRIL##  
 L132 1723 SEA FILE=EMBASE ABB=ON PLU=ON TRAND!L!PRIL##  
 L209 6308 SEA FILE=DRUGU ABB=ON PLU=ON (L124 OR L125 OR L126 OR L127  
 OR L128 OR L129 OR L130 OR L131 OR L132)  
 L210 19007 SEA FILE=DRUGU ABB=ON PLU=ON ACE INHIBITOR?  
 L211 2457 SEA FILE=DRUGU ABB=ON PLU=ON ANGIOTENSIN CONVERTING ENZYME  
 INHIBITOR  
 L212 8522 SEA FILE=DRUGU ABB=ON PLU=ON PATCH?  
 L213 90 SEA FILE=DRUGU ABB=ON PLU=ON (L209 OR L210 OR L211) AND L212  
  
 L214 14371 SEA FILE=DRUGU ABB=ON PLU=ON MATRIX? OR MATRIC?  
 L215 1 SEA FILE=DRUGU ABB=ON PLU=ON L214 AND L213  
 L216 2850 SEA FILE=DRUGU ABB=ON PLU=ON SILICON?  
 L217 0 SEA FILE=DRUGU ABB=ON PLU=ON L216 AND L213  
 L218 6737 SEA FILE=DRUGU ABB=ON PLU=ON (PERMEAT? OR PENETRAT?) (1A)  
 ENHANC?  
 L219 1 SEA FILE=DRUGU ABB=ON PLU=ON L218 AND L213  
 L220 1886 SEA FILE=DRUGU ABB=ON PLU=ON ADHESIV?  
 L221 1 SEA FILE=DRUGU ABB=ON PLU=ON L220 AND L213  
 L222 0 SEA FILE=DRUGU ABB=ON PLU=ON BANDAG? AND L213  
 L223 2 SEA FILE=DRUGU ABB=ON PLU=ON PLASTER? AND L213  
 L230 1 SEA FILE=DRUGU ABB=ON PLU=ON KLOKKERS K?/AU  
 L231 85 SEA FILE=DRUGU ABB=ON PLU=ON KRAMER K?/AU  
 L232 95 SEA FILE=DRUGU ABB=ON PLU=ON FISCHER W?/AU  
 L233 8 SEA FILE=DRUGU ABB=ON PLU=ON SENDL A?/AU  
 L234 0 SEA FILE=DRUGU ABB=ON PLU=ON SENDL LANG A?/AU  
 L238 0 SEA FILE=DRUGU ABB=ON PLU=ON (L230 OR L231 OR L232 OR L233  
 OR L234) AND (L215 OR L217 OR L219 OR (L221 OR L222 OR L223))

=> file wpiX

FILE 'WPIX' ENTERED AT 14:48:22 ON 07 JUL 2006  
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FILE LAST UPDATED: 6 JUL 2006 <20060706/UP>  
 MOST RECENT DERWENT UPDATE: 200643 <200643/DW>  
 DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,  
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[http://www.stn-international.de/training\\_center/patents/stn\\_guide.pdf](http://www.stn-international.de/training_center/patents/stn_guide.pdf) <

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[http://www.stn-international.de/stndatabases/details/ipc\\_reform.html](http://www.stn-international.de/stndatabases/details/ipc_reform.html) and  
<http://scientific.thomson.com/media/scpdf/ipcrdwpi.pdf> <<<

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[http://www.stn-international.de/stndatabases/details/dwpi\\_r.html](http://www.stn-international.de/stndatabases/details/dwpi_r.html) <<<  
 'BIX' IS DEFAULT SEARCH FIELD FOR 'WPIX' FILE

=> d que nos L240

L230 1 SEA FILE=DRUGU ABB=ON PLU=ON KLOKKERS K?/AU  
 L231 85 SEA FILE=DRUGU ABB=ON PLU=ON KRAMER K?/AU

L232 95 SEA FILE=DRUGU ABB=ON PLU=ON FISCHER W?/AU  
 L233 8 SEA FILE=DRUGU ABB=ON PLU=ON SENDL A?/AU  
 L234 0 SEA FILE=DRUGU ABB=ON PLU=ON SENDL LANG A?/AU  
 L235 0 SEA FILE=DRUGU ABB=ON PLU=ON L230 AND (L231 OR L232 OR L233  
 OR L234)  
 L236 0 SEA FILE=DRUGU ABB=ON PLU=ON L231 AND (L232 OR L233 OR L234)  
 L237 0 SEA FILE=DRUGU ABB=ON PLU=ON L232 AND (L233 OR L234)  
 L240 21 SEA FILE=WPIX ABB=ON PLU=ON (L235 OR L236 OR L237)

=> d que nos L253

L230 1 SEA FILE=DRUGU ABB=ON PLU=ON KLOKKERS K?/AU  
 L231 85 SEA FILE=DRUGU ABB=ON PLU=ON KRAMER K?/AU  
 L232 95 SEA FILE=DRUGU ABB=ON PLU=ON FISCHER W?/AU  
 L233 8 SEA FILE=DRUGU ABB=ON PLU=ON SENDL A?/AU  
 L234 0 SEA FILE=DRUGU ABB=ON PLU=ON SENDL LANG A?/AU  
 L235 0 SEA FILE=DRUGU ABB=ON PLU=ON L230 AND (L231 OR L232 OR L233  
 OR L234)  
 L236 0 SEA FILE=DRUGU ABB=ON PLU=ON L231 AND (L232 OR L233 OR L234)  
 L237 0 SEA FILE=DRUGU ABB=ON PLU=ON L232 AND (L233 OR L234)  
 L240 21 SEA FILE=WPIX ABB=ON PLU=ON (L235 OR L236 OR L237)  
 L242 970 SEA FILE=WPIX ABB=ON PLU=ON B14-F02B1/MC  
 L243 882 SEA FILE=WPIX ABB=ON PLU=ON B12-F05A/MC  
 L244 16 SEA FILE=WPIX ABB=ON PLU=ON C14-F02B1/MC  
 L245 27 SEA FILE=WPIX ABB=ON PLU=ON C12-F05A/MC  
 L246 1852 SEA FILE=WPIX ABB=ON PLU=ON (L242 OR L243 OR L244 OR L245)  
 L247 3767 SEA FILE=WPIX ABB=ON PLU=ON B12-M02D/MC  
 L248 4457 SEA FILE=WPIX ABB=ON PLU=ON B12-M02F/MC  
 L249 278 SEA FILE=WPIX ABB=ON PLU=ON C12-M02F/MC  
 L250 209 SEA FILE=WPIX ABB=ON PLU=ON C12-M02D/MC  
 L251 7446 SEA FILE=WPIX ABB=ON PLU=ON (L247 OR L248 OR L249 OR L250)  
 L252 16 SEA FILE=WPIX ABB=ON PLU=ON L246 AND L251  
 L253 2 SEA FILE=WPIX ABB=ON PLU=ON L240 AND L252

=> s L240 or L253

L256 21 L240 OR L253

=> => dup rem L58 L254 L255 L208 L238 L256

L238 HAS NO ANSWERS

FILE 'HCAPLUS' ENTERED AT 14:49:46 ON 07 JUL 2006

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PROCESSING COMPLETED FOR L58

PROCESSING COMPLETED FOR L254  
 PROCESSING COMPLETED FOR L255  
 PROCESSING COMPLETED FOR L208  
 PROCESSING COMPLETED FOR L238  
 PROCESSING COMPLETED FOR L256

L257 43 DUP REM L58 L254 L255 L208 L238 L256 (18 DUPLICATES REMOVED)

ANSWERS '1-20' FROM FILE HCAPLUS  
 ANSWERS '21-22' FROM FILE MEDLINE  
 ANSWERS '23-25' FROM FILE EMBASE  
 ANSWERS '26-39' FROM FILE BIOSIS  
 ANSWERS '40-43' FROM FILE WPIX

=> d ibib abs hitind hitstr L257 1-20; d iall L257 21-43

L257 ANSWER 1 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1

ACCESSION NUMBER: 2002:51249 HCAPLUS

DOCUMENT NUMBER: 136:107528

TITLE: Matrix controlled transdermal system for stable derivatives of ACE inhibitors

INVENTOR(S): Klokke, Karin; Kramer, Kai-Thomas  
 ; Fischer, Wilfried; Sendl-Lang, Anna

PATENT ASSIGNEE(S): Hexal A.-G., Germany

SOURCE: PCT Int. Appl., 23 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002003970	A2	20020117	WO 2001-EP8071	20010712
WO 2002003970	A3	20020523		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
DE 10033855	A1	20020131	DE 2000-10033855	20000712
CA 2415476	AA	20030109	CA 2001-2415476	20010712
EP 1299091	A2	20030409	EP 2001-960496	20010712
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
JP 2004502726	T2	20040129	JP 2002-508425	20010712
US 2004052835	A1	20040318	US 2003-19121	20030516
PRIORITY APPLN. INFO.:			DE 2000-10033855	A 20000712
			WO 2001-EP8071	W 20010712

AB The invention relates to a matrix controlled transdermal therapeutic system comprising, (i) a top layer which is impervious to active ingredients, (ii) a self adhesive matrix layer or several matrix layers, whereby at least the exposed matrix layer is self adhesive when the system is applied, or comprising one or several matrix layers with adhesive surfaces. The matrix layers contain at least one ACE inhibitor (angiotensin converting enzyme inhibitor); its metabolite is a dicarboxylic acid selected from the following group: diesters, a di-salt

which is obtainable with one or several bases and a mono-salt which is obtainable with one or several acids and (iii) a tear-off protective layer. Thus a transdermal patch contained (w/matrix w%): trandolapril 10; methanesulfonic acid 2.4; Aerosil 200 4; Cetirol HE 10; Durotak 387-2353 73.6.

IC ICM A61K009-70  
ICS A61K038-55  
CC 63-6 (Pharmaceuticals)

L257 ANSWER 2 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 2002:51248 HCAPLUS  
DOCUMENT NUMBER: 136:123635  
TITLE: Transdermal therapeutic systems with highly dispersed silicon dioxide  
INVENTOR(S): Klokke, Karin; Kramer, Kai-Thomas  
; Wilhelm, Martina  
PATENT ASSIGNEE(S): Hexal A.-G., Germany  
SOURCE: PCT Int. Appl., 28 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: German  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002003969	A2	20020117	WO 2001-EP8070	20010712
WO 2002003969	A3	20020523		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 10033853	A1	20020131	DE 2000-10033853	20000712
CA 2415658	AA	20020117	CA 2001-2415658	20010712
EP 1301179	A2	20030416	EP 2001-951670	20010712
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004502725	T2	20040129	JP 2002-508424	20010712
US 2004086552	A1	20040506	US 2003-332864	20030228
PRIORITY APPLN. INFO.: DE 2000-10033853 A 20000712				
WO 2001-EP8070 W 20010712				
AB The invention relates to a transdermal therapeutic system comprising a surface layer which is impermeable with respect to an active ingredient; a self-adherent matrix layer or a plurality of matrix layers; the matrix layer is self-adherent when the system is applied. The system also comprises a pull-off protective cover; the matrix layer(s) contain(s) one or more active ingredients and/or one or more biol. active substances and highly dispersed silicon dioxide. The system contains silicon dioxide in order to increase skin permeation. Thus a transdermal system contained (w/matrix w%): trandolapril 10; Eutanol G 10; Polyisobutylene adhesive MA24A 76; Aerosil 200 4; after 24 h penetration values of 37.50-58.0 µg/cm <sup>2</sup> was measured; the value is higher than for similar transdermal system without silicon dioxide (4.9-14.4 µg/cm <sup>2</sup> ).				
IC ICM A61K009-70				
ICS A61K047-02				

CC 63-6 (Pharmaceuticals)

L257 ANSWER 3 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 3  
 ACCESSION NUMBER: 2000:95996 HCAPLUS  
 DOCUMENT NUMBER: 132:141962  
 TITLE: Pharmaceutical composition containing cyclosporin A  
 INVENTOR(S): Klokke, Karin; Fischer, Wilfried  
 PATENT ASSIGNEE(S): Hexal A.-G., Germany  
 SOURCE: U.S., 5 pp., Cont.-in-part of U.S. Ser. No. 633,823,  
 abandoned.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6022852	A	20000208	US 1998-76175	19980511
PRIORITY APPLN. INFO.:			DE 1993-4336163	A 19931022
			US 1996-633823	B2 19960627

AB The invention relates to a pharmaceutical composition consisting of cyclosporin A and  $\alpha$ -tocopherol or one of the derivs. thereof. The invention is based on the finding that  $\alpha$ -tocopherol and its derivs. have an excellent dissolving capacity for cyclosporin A. An injection concentrate contained cyclosporin A 50, tocopherol (Copherol F1300) 100, lecithin 200, ethanol 100, and eutanol 500 mg.

IC ICM A61K038-00  
 ICS A61K031-355

INCL 514011000

CC 63-6 (Pharmaceuticals)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L257 ANSWER 4 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 4

ACCESSION NUMBER: 1999:460340 HCAPLUS  
 DOCUMENT NUMBER: 131:92527  
 TITLE: Pharmaceutical composition comprising  
 Z-4-hydroxytamoxifen and cyclodextrin  
 INVENTOR(S): Fischer, Wilfried; Klokke, Karin  
 ; Sendl-Lang, Anna  
 PATENT ASSIGNEE(S): Hexal A.-G., Germany  
 SOURCE: PCT Int. Appl., 12 pp.  
 CODEN: PIXXD2

DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9933451	A2	19990708	WO 1998-EP8437	19981223
WO 9933451	A3	19990910		
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,			

CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9925138	A1	19990719	AU 1999-25138	19981223
EP 1043986	A2	20001018	EP 1998-966848	19981223
EP 1043986	B1	20030416		
R: DE, FR, GB, NL				
JP 2001527037	T2	20011225	JP 2000-526208	19981223
PRIORITY APPLN. INFO.:			EP 1997-122742	A 19971223
			WO 1998-EP8437	W 19981223

AB The invention concerns a mixture and a pharmaceutical composition consisting of Z-4-hydroxytamoxifen and at least 1 cyclodextrin. Thus, a complex was obtained by the treatment of 4-hydroxytamoxifen and cyclodextrin with  $\gamma$ -cyclodextrin in pH 7 physiolo. saline solution The storage stability of the complex was demonstrated.

IC ICM A61K031-00  
CC 63-6 (Pharmaceuticals)

L257 ANSWER 5 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 5

ACCESSION NUMBER: 1999:7800 HCAPLUS  
DOCUMENT NUMBER: 130:57229  
TITLE: Controlled release pharmaceutical preparation with ACE inhibitor as active agent  
INVENTOR(S): Fischer, Wilfried; Klokke, Karin  
; Oppelt, Renate  
PATENT ASSIGNEE(S): Hexal Ag, Germany  
SOURCE: PCT Int. Appl., 23 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: German  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9856355	A1	19981217	WO 1998-EP3536	19980612
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
DE 19724696	A1	19981224	DE 1997-19724696	19970612
CA 2295013	AA	19981217	CA 1998-2295013	19980612
AU 9883368	A1	19981230	AU 1998-83368	19980612
AU 736357	B2	20010726		
ZA 9805142	A	20000112	ZA 1998-5142	19980612
EP 994696	A1	20000426	EP 1998-933605	19980612
EP 994696	B1	20040218		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI				
TR 9903069	T2	20000522	TR 1999-3069	19980612
NZ 501726	A	20010928	NZ 1998-501726	19980612
JP 2002504108	T2	20020205	JP 1999-501625	19980612
AT 259637	E	20040315	AT 1998-933605	19980612
ES 2216296	T3	20041016	ES 1998-933605	19980612
NO 9906049	A	20000207	NO 1999-6049	19991208
US 6267990	B1	20010731	US 1999-460055	19991213
PRIORITY APPLN. INFO.:			DE 1997-19724696	A 19970612
			WO 1998-EP3536	W 19980612

AB The title preparation contains: (i) an initial dose of active agent and optional auxiliary agents, (ii) a 1st type of controlled-release pellet in which the active agent and optional auxiliary agents are coated, and (iii) a 2nd type of controlled-release pellet in which the active agent and optional auxiliary agents are also coated. The weight ratio of the masses of the coatings in (ii) and (iii) is (1:2)-(1:7). This preparation allows an almost immediate action of the ACE inhibitor (e.g. captopril) without a marked initial peak in blood level, and maintenance of a long-lasting therapeutic blood level of the drug thereafter with very little variation. Thus, pellets A were prepared containing captopril 5, Avicel (microcryst. cellulose) 3, and tablettose 2 mg. Pellets A (700 g) were coated with Opadry II 40.48 and H2O 250 g, followed by a 2nd coat containing Eudragit S 100 62.5, di-Bu phthalate 6.25, 96% EtOH 350.00, and H2O 87.5 g to produce pellets B. Addnl. pellets A (700 g) were coated with Opadry II and H2O as above, followed by a coating of Eudragit S 100 192.5, di-Bu phthalate 19.25, 96% EtOH 1078, and H2O 269.5 g to produce pellets C. Pellets A 100, pellets B 700, and pellets C 700 g were dispensed into a gelatin capsule with a final captopril content of 150 mg.

IC ICM A61K009-16

ICS A61K009-56; A61K038-55

CC 63-6 (Pharmaceuticals)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L257 ANSWER 6 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 6

ACCESSION NUMBER: 1998:621112 HCAPLUS

DOCUMENT NUMBER: 129:235662

TITLE: Stabilization of acid sensitive benzimidazoles with amino acid/cyclodextrin combinations

INVENTOR(S): Klokke, Karin; Kutschera, Marion; Fischer, Wilfried

PATENT ASSIGNEE(S): Hexal A.-G., Germany

SOURCE: PCT Int. Appl., 21 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9840069	A2	19980917	WO 1998-EP1478	19980313
WO 9840069	A3	19981217		
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW			
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
CA 2282513	AA	19980917	CA 1998-2282513	19980313
AU 9872070	A1	19980929	AU 1998-72070	19980313
AU 731186	B2	20010329		
ZA 9802155	A	19981201	ZA 1998-2155	19980313
EP 991407	A2	20000412	EP 1998-919099	19980313
EP 991407	B1	20011128		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI			
BR 9808581	A	20000530	BR 1998-8581	19980313

NZ 337592	A	20010126	NZ 1998-337592	19980313
JP 2001518083	T2	20011009	JP 1998-539237	19980313
AT 209491	E	20011215	AT 1998-919099	19980313
ES 2167891	T3	20020516	ES 1998-919099	19980313
PT 991407	T	20020531	PT 1998-919099	19980313
CZ 291842	B6	20030618	CZ 1999-3128	19980313
CN 1113649	B	20030709	CN 1998-803296	19980313
SK 284811	B6	20051201	SK 1999-1209	19980313
US 6248758	B1	20010619	US 1999-319895	19990908
NO 9904409	A	19991021	NO 1999-4409	19990910
HK 1024182	A1	20040305	HK 2000-103624	20000616

## PRIORITY APPLN. INFO.:

EP 1997-104200	A	19970313
WO 1998-EP1478	W	19980313

AB A pharmaceutical formulation comprising or consisting of a benzimidazole derivative as active ingredient, and as excipients, at least one cyclodextrin and at least one amino acid is disclosed. Omeprazole 1.32, L-arginine (I) 0.68, and  $\beta$ -cyclodextrin (II) 10.56 g were powdered, then kneaded with 3 mL of water for a few minutes. The resulting paste was dried at room temperature overnight in a vacuum desiccator. The powder had an off-white color

while the controls without I or II were brown.

IC ICM A61K031-44

ICS A61K009-16; A61K047-18

CC 63-6 (Pharmaceuticals)

L257 ANSWER 7 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 7

ACCESSION NUMBER: 1998:38370 HCAPLUS

DOCUMENT NUMBER: 128:93212

TITLE: Plaster for transdermal application of pergolide

INVENTOR(S): Fischer, Wilfried; Sendl-Lang, Anna  
; Zeh-Herwerth, Dagmar

PATENT ASSIGNEE(S): Hexal A.-G., Germany

SOURCE: Ger. Offen., 4 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19626621	A1	19980108	DE 1996-19626621	19960702
CA 2259353	AA	19980108	CA 1997-2259353	19970702
WO 9800142	A1	19980108	WO 1997-EP3458	19970702
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9736926	A1	19980121	AU 1997-36926	19970702
AU 727267	B2	20001207		
EP 910379	A1	19990428	EP 1997-933646	19970702
EP 910379	B1	20030423		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI				
JP 2000514053	T2	20001024	JP 1998-503851	19970702
AT 238054	E	20030515	AT 1997-933646	19970702
ES 2198584	T3	20040201	ES 1997-933646	19970702

US 6623752 B1 20030923 US 2000-550926 20000417  
 PRIORITY APPLN. INFO.: DE 1996-19626621 A 19960702  
 WO 1997-EP3458 W 19970702  
 US 1998-214209 B1 19981230

AB A transdermal plaster for systemic administration of pergolide or a pergolide salt, optionally in combination with  $\geq 1$  addnl. drugs such as another dopamine agonist, comprises an impermeable backing layer, an active agent-containing reservoir layer, an optional semipermeable membrane, and a detachable release liner. The reservoir layer may constitute a self-adhesive matrix or may be covered with an adhesive coating. Thus, a dispersion of pergolide 10, vitamin E 10, propylene glycol 15, and 35% EtOAc solution of acrylate adhesive (e.g. Duro-Tak 326-1753) was spread on a siliconized polypropylene film to a dry surface d. of 100 g/m<sup>2</sup>, laminated with 50- $\mu$ m polyurethane film, and cut into plasters 20 cm<sup>2</sup> in area.

IC ICM A61L015-44

ICS A61L015-22; A61K031-48; A61K031-195; A61K031-44; A61M037-00

CC 63-6 (Pharmaceuticals)

L257 ANSWER 8 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 8

ACCESSION NUMBER: 1997:650256 HCAPLUS

DOCUMENT NUMBER: 127:298750

TITLE: Diclofenac- $\gamma$ -cyclodextrin inclusion compounds for oral dosage forms

INVENTOR(S): Fischer, Wilfried; Sendl-Lang, Anna

PATENT ASSIGNEE(S): Hexal A.-G., Germany; Fischer, Wilfried; Sendl-Lang, Anna

SOURCE: PCT Int. Appl., 21 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9735568	A2	19971002	WO 1997-EP1595	19970327
WO 9735568	A3	19971204		
W:	AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
CA 2250009	AA	19971002	CA 1997-2250009	19970327
AU 9723829	A1	19971017	AU 1997-23829	19970327
AU 713902	B2	19991216		
ZA 9702707	A	19971022	ZA 1997-2707	19970327
EP 893994	A2	19990203	EP 1997-919309	19970327
EP 893994	B1	20020220		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI			
CN 1217658	A	19990526	CN 1997-194134	19970327
BR 9708280	A	19990803	BR 1997-8280	19970327
JP 2000507258	T2	20000613	JP 1997-534053	19970327
AT 213410	E	20020315	AT 1997-919309	19970327
US 6071964	A	20000606	US 1999-155298	19990511

PRIORITY APPLN. INFO.: HU 1996-758 A 19960327  
 WO 1997-EP1595 W 19970327

AB The object of the present invention is an oral drug preparation containing the

the  $\gamma$ -cyclodextrin complex of diclofenac (or pharmaceutically acceptable salts thereof, especially sodium salt) prepared by known methods and by which

gastrointestinal irritancy of diclofenac can be considerably decreased. Diclofenac sodium- $\gamma$ -cyclodextrin inclusion compound (1:2) was given orally to rats for 4 days; both in the inclusion compd-treated groups and diclofenac Na-treated groups perforations were observed in the jejunoileal part of the small intestine; however, the irritancy index was significantly lower in the case of the inclusion compound-treated rats than in the diclofenac Na-treated group.

IC ICM A61K031-19  
ICS A61K047-48  
CC 63-6 (Pharmaceuticals)

L257 ANSWER 9 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 9

ACCESSION NUMBER: 1997:276512 HCAPLUS  
DOCUMENT NUMBER: 126:255524  
TITLE: Tacrine patch  
INVENTOR(S): Sendl-Lang, Anna; Fischer, Wilfried  
PATENT ASSIGNEE(S): Hexal Ag, Germany; Sendl-Lang, Anna; Fischer, Wilfried  
SOURCE: PCT Int. Appl., 23 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: German  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9709969	A1	19970320	WO 1996-EP4010	19960912
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
DE 19533772	C1	19980102	DE 1995-19533772	19950912
AU 9671287	A1	19970401	AU 1996-71287	19960912
EP 850052	A1	19980701	EP 1996-932512	19960912
EP 850052	B1	20011212		
R: CH, DE, FR, GB, LI				

PRIORITY APPLN. INFO.: DE 1995-19533772 A 19950912  
WO 1996-EP4010 W 19960912

AB A transdermal patch is provided for administration of tacrine at a constant rate for treatment of Alzheimer's disease. This route of administration avoids the marked 1st-pass metabolism, fluctuating pharmacokinetics, and rapid elimination of orally administered tacrine. The skin permeability to tacrine is improved by use of selegiline and a mixture of hydrophilic and lipophilic solvents of low volatility. Thus, a solution of tacrine and selegiline in EtOH was mixed with a solution of Duro-Tak 326-1753 (acrylate adhesive) in EtOAc/hexane; the mixture was spread to a wet thickness of 450  $\mu$ m on siliconized polyester film, dried at 50° for 1 h, covered with a polyester release liner, and cut into patches.

IC ICM A61K009-70  
CC 63-6 (Pharmaceuticals)

L257 ANSWER 10 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 10

ACCESSION NUMBER: 1997:283770 HCAPLUS  
DOCUMENT NUMBER: 126:268531

TITLE: Tacrine patch  
 INVENTOR(S): Sendl-Lang, Anna; Fischer, Wilfried  
 PATENT ASSIGNEE(S): Hexal Ag, Germany; Sendl-Lang, Anna; Fischer, Wilfried  
 SOURCE: PCT Int. Appl., 14 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9709050	A2	19970313	WO 1996-EP3917	19960906
WO 9709050	A3	19970605		
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
DE 19533089	C1	19970522	DE 1995-19533089	19950907
ZA 9607553	A	19970325	ZA 1996-7553	19960906
AU 9671267	A1	19970327	AU 1996-71267	19960906
EP 848611	A2	19980624	EP 1996-932478	19960906
EP 848611	B1	20010718		

R: CH, DE, FR, GB, LI

PRIORITY APPLN. INFO.: DE 1995-19533089 A 19950907  
 WO 1996-EP3917 W 19960906

AB A transdermal patch is provided for administration of tacrine at a constant rate for treatment of Alzheimer's disease. This route of administration avoids the marked 1st-pass metabolism, fluctuating pharmacokinetics, and rapid elimination of orally administered tacrine. The skin permeability to tacrine is improved by use of a mixture of hydrophilic and lipophilic solvents of low volatility. Thus, a solution of tacrine in EtOH was mixed with a solution of Duro-Tak 326-1753 (acrylate adhesive) in EtOAc/hexane; the mixture was spread to a wet thickness of 450 µm on siliconized polyester film, dried at 50° for 1 h, covered with a polyester release liner, and cut into patches.

IC ICM A61K031-645  
 ICS A61K031-47; A61K009-70  
 CC 63-6 (Pharmaceuticals)

L257 ANSWER 11 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 11

ACCESSION NUMBER: 1997:90478 HCAPLUS

DOCUMENT NUMBER: 126:108925

TITLE: Liquid cyclosporin A preparation for oral or topical administration

INVENTOR(S): Klokke, Karin; Fischer, Wilfried

PATENT ASSIGNEE(S): Hexal Pharmaforschung GmbH, Germany

SOURCE: Ger. Offen., 6 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19521974	A1	19961219	DE 1995-19521974	19950616

CA 2224792 AA 19970103 CA 1996-2224792 19960613  
 CA 2224792 C 20030107  
 WO 9700080 A1 19970103 WO 1996-EP2559 19960613  
 W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE,  
 ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT,  
 LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,  
 SG, SI  
 RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR,  
 IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN  
 AU 9663556 A1 19970115 AU 1996-63556 19960613  
 AU 705155 B2 19990513  
 EP 833655 A1 19980408 EP 1996-922803 19960613  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI  
 ZA 9605087 A 19970122 ZA 1996-5087 19960614  
 US 2001014665 A1 20010816 US 1998-204782 19981203  
 US 6696413 B2 20040224  
 PRIORITY APPLN. INFO.: DE 1995-19521974 A 19950616  
 WO 1996-EP2559 W 19960613  
 US 1997-981630 B1 19971216

AB Cyclosporin A is formulated in solution or emulsion form with an  
 $\alpha$ -tocopherol derivative as emulsifier, an ethoxylated plant oil, fatty  
 acid, or fat as coemulsifier, and an alc. for administration topically for  
 treatment of psoriasis, or orally as an immunosuppressant. This  
 formulation shows reduced nephrotoxicity and increased permeation through  
 the skin. Thus, gelatin capsules were filled with a mixture of cyclosporin  
 A 100, 96% EtOH 200, D- $\alpha$ -tocopherol PEG-1000 succinate 300,  
 ethoxylated castor oil 200, and PEG-400 200 mg.

IC ICM A61K038-13  
 CC 63-6 (Pharmaceuticals)

L257 ANSWER 12 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 12  
 ACCESSION NUMBER: 1995:645248 HCAPLUS  
 DOCUMENT NUMBER: 123:40956  
 TITLE: Pharmaceutical composition containing cyclosporin A  
 and  $\alpha$ -tocopherol  
 INVENTOR(S): Klokke, Karin; Fischer, Wilfried  
 PATENT ASSIGNEE(S): Hexal Pharma GmbH, Germany  
 SOURCE: PCT Int. Appl., 18 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9511039	A1	19950427	WO 1994-EP3274	19940930
W: JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 724452	A1	19960807	EP 1994-928852	19940930
EP 724452	B1	20000524		
R: CH, DE, ES, FR, GB, IT, LI, NL				
JP 09504012	T2	19970424	JP 1995-511237	19940930
JP 3644543	B2	20050427		
ES 2148345	T3	20001016	ES 1994-928852	19940930
PRIORITY APPLN. INFO.:			DE 1993-4336163	A 19931022
			WO 1994-EP3274	W 19940930

AB A pharmaceutical composition contains cyclosporin A and  $\alpha$ -tocopherol or  
 one of its derivs. as solubilizer.  $\alpha$ -Tocopherol also improves  
 resorption of cyclosporin A through the skin and diminishes the

nephrotoxicity of cyclosporin A by inhibiting prostanoid synthesis. Thus, a soft gelatin capsule contained cyclosporin A 125, EtOH 125, D- $\alpha$ -tocopherol 325, and D- $\alpha$ -tocopherol PEG-1000 succinate 425 mg.

IC ICM A61K038-13  
ICI A61K038-13, A61K031-355  
CC 63-6 (Pharmaceuticals)

L257 ANSWER 13 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 13  
ACCESSION NUMBER: 1995:902921 HCAPLUS  
DOCUMENT NUMBER: 123:296666  
TITLE: Delayed-release tablet containing diclofenac sodium  
INVENTOR(S): Fischer, Wilfried; Klokke, Karin  
PATENT ASSIGNEE(S): Hexal Pharma GmbH, Germany  
SOURCE: Ger. Offen., 7 pp.  
CODEN: GWXXBX  
DOCUMENT TYPE: Patent  
LANGUAGE: German  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4408326	A1	19950914	DE 1994-4408326	19940311
CA 2185242	AA	19950914	CA 1995-2185242	19950313
CA 2185242	C	20041123		
WO 9524188	A1	19950914	WO 1995-EP928	19950313
W: AU, CA, CZ, FI, JP, NO, PL, SK, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9520695	A1	19950925	AU 1995-20695	19950313
AU 692534	B2	19980611		
EP 749304	A1	19961227	EP 1995-913097	19950313
EP 749304	B1	19981118		
EP 749304	B2	20040303		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
JP 09509953	T2	19971007	JP 1995-523249	19950313
AT 173399	E	19981215	AT 1995-913097	19950313
ES 2126265	T3	19990316	ES 1995-913097	19950313
PL 177607	B1	19991231	PL 1995-316196	19950313
FI 9603567	A	19960910	FI 1996-3567	19960910
NO 9603796	A	19961106	NO 1996-3796	19960910
NO 317396	B1	20041025		
US 5874107	A	19990223	US 1996-714063	19960911
PRIORITY APPLN. INFO.:			DE 1994-4408326	A 19940311
			WO 1995-EP928	W 19950313

AB A delayed-release tablet contains hydroxypropylmethylcellulose as retarding agent and diclofenac Na as active agent in a proportion of >0.3:1. Thus, a delayed-release tablet contained diclofenac Na 125.0, lactose.H<sub>2</sub>O 70.4, hydroxypropylmethylcellulose 122.5, dye 0.1, Mg stearate 3.5, and highly disperse SiO<sub>2</sub> 3.5 mg. This tablet could be coated with a layer providing high initial release of diclofenac Na, containing diclofenac Na 25.0, lactose.H<sub>2</sub>O 15.0, CaHPO<sub>4</sub>.2H<sub>2</sub>O 20.0, microcryst. cellulose 24.5, corn starch 10.0, Na CM-starch 4.0, Mg stearate 1.0, and highly disperse SiO<sub>2</sub> 0.5 mg.

IC ICM A61K009-22  
ICS A61K031-557  
CC 63-6 (Pharmaceuticals)

L257 ANSWER 14 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 14  
ACCESSION NUMBER: 1995:708816 HCAPLUS

DOCUMENT NUMBER: 123:93339  
 TITLE: Plaster for transdermal administration of tamoxifen derivative  
 INVENTOR(S): Fischer, Wilfried; Klokke, Karin  
 PATENT ASSIGNEE(S): Hexal Pharma GmbH, Germany  
 SOURCE: Ger., 4 pp.  
 CODEN: GWXXAW  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4407742	C1	19950622	DE 1994-4407742	19940308
CA 2185016	AA	19950914	CA 1995-2185016	19950220
WO 9524187	A1	19950914	WO 1995-EP603	19950220
W: AU, CA, CZ, FI, JP, NO, PL, SK, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9518106	A1	19950925	AU 1995-18106	19950220
AU 694184	B2	19980716		
EP 748218	A1	19961218	EP 1995-909746	19950220
EP 748218	B1	20010801		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
JP 09509948	T2	19971007	JP 1995-523185	19950220
AT 203667	E	20010815	AT 1995-909746	19950220
ZA 9501880	A	19951211	ZA 1995-1880	19950307
FI 9603515	A	19960906	FI 1996-3515	19960906

PRIORITY APPLN. INFO.: DE 1994-4407742 A 19940308  
 WO 1995-EP603 W 19950220

AB A reservoir-type transdermal dosage system contains a tamoxifen derivative, e.g. 3- or 4-hydroxytamoxifen, dissolved in an alc. or a water-alc. mixture to enhance resorption. Addition of vitamin E further enhances resorption.  
 IC ICM A61L015-44  
 ICS A61F013-02; A61K031-135; A61M037-00  
 CC 63-6 (Pharmaceuticals)

L257 ANSWER 15 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 15

ACCESSION NUMBER: 1995:682889 HCAPLUS  
 DOCUMENT NUMBER: 123:65859  
 TITLE: A stable prostaglandin E1 preparation for therapeutic use  
 INVENTOR(S): Fischer, Wilfried; Klokke, Karin  
 PATENT ASSIGNEE(S): Hexal Pharma GmbH, Germany  
 SOURCE: Ger. Offen., 3 pp.  
 CODEN: GWXXBX  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4342232	A1	19950614	DE 1993-4342232	19931210
PRIORITY APPLN. INFO.:			DE 1993-4342232	19931210

AB A title preparation can be made by adding to 2500 mL water for injection 50 mg prostaglandin E1, 3235 g  $\alpha$ -cyclodextrin, and 250 g lactose x 1H<sub>2</sub>O. The mixture is placed in ampules and lyophilized. After freeze-drying, the ampules are removed from the drier and placed at room temperature in an atmospheric of

50% rel. humidity and sealed after a certain period of time. The stability of the product is greater with a water content of 2% than with a water content of 0.7% or less. With a water content of 1.92%, the content of prostaglandin A1 (a breakdown product of prostaglandin E1) was less than 0.2% after 6 mo, the same as at time zero.

IC ICM A61K031-557  
CC 63-6 (Pharmaceuticals)

L257 ANSWER 16 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 16

ACCESSION NUMBER: 1995:645321 HCAPLUS  
DOCUMENT NUMBER: 123:40975  
TITLE: Tablets or capsules containing ranitidine hydrochloride form 1  
INVENTOR(S): Fischer, Wilfried; Klokke, Karin  
PATENT ASSIGNEE(S): Hexal Pharma GmbH, Germany  
SOURCE: Ger. Offen., 3 pp.  
CODEN: GWXXBX  
DOCUMENT TYPE: Patent  
LANGUAGE: German  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4341310	A1	19950608	DE 1993-4341310	19931203
WO 9515162	A1	19950608	WO 1994-EP4044	19941205
W: AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9512423	A1	19950619	AU 1995-12423	19941205
EP 731701	A1	19960918	EP 1995-903320	19941205
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
US 5910320	A	19990608	US 1996-652439	19960819
PRIORITY APPLN. INFO.: DE 1993-4341310 A 19931203				
WO 1994-EP4044 W 19941205				

AB Tablets or capsules are prepared from a powdered mixture containing stable ranitidine-HCl form 1, a carrier, and diluents. Thus, tablets were prepared containing ranitidine-HCl 336, Aerosil 5, Promojel 15, Emcocel 80, Emcanpress 31, corn starch 25, talc 5, and Mg stearate 3 mg.

IC ICM A61K031-34  
ICS A61K009-20; A61K009-48  
CC 63-6 (Pharmaceuticals)

L257 ANSWER 17 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 17

ACCESSION NUMBER: 1995:252597 HCAPLUS  
DOCUMENT NUMBER: 122:17230  
TITLE: Vitamin E as penetration enhancer in active substance-containing plaster  
INVENTOR(S): Fischer, Wilfried; Klokke, Karin  
PATENT ASSIGNEE(S): Hexal Pharma GmbH, Germany  
SOURCE: PCT Int. Appl., 38 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 9423707	A1	19941027	WO 1994-EP1231	19940420
W: AU, CA, FI, HU, JP, NO, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 4339400	A1	19950524	DE 1993-4339400	19931118
CA 2161004	AA	19941027	CA 1994-2161004	19940420
CA 2161004	C	20041026		
AU 9465696	A1	19941108	AU 1994-65696	19940420
AU 678237	B2	19970522		
ZA 9402730	A	19951020	ZA 1994-2730	19940420
EP 695177	A1	19960207	EP 1994-913616	19940420
EP 695177	B1	19980218		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
HU 73668	A2	19960930	HU 1995-2994	19940420
JP 09501398	T2	19970210	JP 1994-522784	19940420
JP 3489831	B2	20040126		
EP 813865	A1	19971229	EP 1997-113342	19940420
EP 813865	B1	20010919		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
AT 163262	E	19980315	AT 1994-913616	19940420
ES 2115231	T3	19980616	ES 1994-913616	19940420
AT 205706	E	20011015	AT 1997-113342	19940420
ES 2164286	T3	20020216	ES 1997-113342	19940420
PT 813865	T	20020228	PT 1997-113342	19940420
FI 9504989	A	19951019	FI 1995-4989	19951019
NO 9504186	A	19951019	NO 1995-4186	19951019
NO 311829	B1	20020204		
US 5683711	A	19971104	US 1995-535038	19951215
PRIORITY APPLN. INFO.:			DE 1993-4312818	A 19930420
			DE 1993-4339400	A 19931118
			EP 1994-913616	A3 19940420
			WO 1994-EP1231	W 19940420

AB An active substance-containing laminated plaster for transdermal drug administration contains a carrier and a matrix made of a single polymer, and if required another polymer, as well as vitamin E to increase the thermodyn. activity of the active substance and improve adhesion to the skin without irritating the skin or causing recrystn. of the supersatd. active substance in the matrix. Thus, a mixture of selegiline 20,  $\alpha$ -tocopherol 20, and Durotak 1753 60 g was spread on a siliconized film to a surface d. of 90 g/m<sup>2</sup>. Permeation of selegiline from this plaster through the skin in vitro was 649  $\mu$ g/2.5 cm<sup>2</sup>/12 h.

IC ICM A61K009-70  
CC 63-6 (Pharmaceuticals)

L257 ANSWER 18 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 18  
ACCESSION NUMBER: 1994:708315 HCAPLUS  
DOCUMENT NUMBER: 121:308315  
TITLE: Crystalline cyclodextrin inclusion complexes of ranitidine hydrochloride and process for their preparation  
INVENTOR(S): Fischer, Wilfried; Klokkeers, Karin  
PATENT ASSIGNEE(S): Hexal Pharma G.m.b.H., Germany  
SOURCE: PCT Int. Appl., 21 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 9420091      A1      19940915      WO 1994-EP645      19940304
W:  CA, CZ, HU, JP, RU, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
CA 2157190      AA      19940915      CA 1994-2157190      19940304
ZA 9401544      A       19941031      ZA 1994-1544         19940304
EP 687174      A1      19951220      EP 1994-909927       19940304
EP 687174      B1      20010613
R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE
JP 09502698     T2      19970318      JP 1994-519579       19940304
RU 2143896      C1      20000110      RU 1995-121629       19940304
US 5665767      A       19970909      US 1995-513779       19951215
H U 1993-6024      A       19930305
WO 1994-EP645      W       19940304
PRIORITY APPLN. INFO.:

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AB The present invention relates to cyclodextrin inclusion complexes of ranitidine hydrochloride which exhibit a novel, to date unknown crystalline structure, being significantly different from those of known "Form 1 and 2" and to the preparation of such inclusion complexes. The inclusion complexes are prepared from aqueous common solution or suspensions of ranitidine hydrochloride and cyclodextrin by removal of water. As complexing agents,  $\alpha$ -,  $\beta$ - and  $\gamma$ -cyclodextrins, their alkylated, hydroxy alkylated derivs. or their suitable mixts. are utilized. Finally, the invention concerns pharmaceutical compns. comprising the new complexes. Ranitidine.HCl- $\beta$ -cyclodextrin complex was prepared by removing water from the solution by freeze-drying or by vacuum drying and then characterized.

IC ICM A61K031-34  
ICS A61K047-48

CC 63-6 (Pharmaceuticals)

L257 ANSWER 19 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1996:664745 HCAPLUS

DOCUMENT NUMBER: 125:285027

TITLE: Device for the transdermal delivery of angiotensin-converting enzyme inhibitors

INVENTOR(S): Fischer, Wilfried; Klokkeers, Karin

PATENT ASSIGNEE(S): Hexal Pharma GmbH, Germany

SOURCE: Ger. Offen., 5 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19512181	A1	19961002	DE 1995-19512181	19950331
DE 19512181	C2	20031106		
CA 2216278	AA	19961003	CA 1996-2216278	19960329
WO 9629999	A1	19961003	WO 1996-EP1402	19960329
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9654982	A1	19961016	AU 1996-54982	19960329
AU 700418	B2	19990107		
EP 817622	A1	19980114	EP 1996-911973	19960329

EP 817622 B1 20011128  
 R: AT, CH, DE, DK, ES, GB, LI, LU, NL, SE, PT, SI, LT, LV  
 JP 11502827 T2 19990309 JP 1996-528948 19960329  
 BR 9607872 A 19991130 BR 1996-7872 19960329  
 NZ 306429 A 20000728 NZ 1996-306429 19960329  
 CZ 287373 B6 20001115 CZ 1997-3028 19960329  
 AT 209482 E 20011215 AT 1996-911973 19960329  
 ES 2167558 T3 20020516 ES 1996-911973 19960329  
 PT 817622 T 20020531 PT 1996-911973 19960329  
 ZA 9602592 A 19971001 ZA 1996-2592 19960401  
 NO 9704508 A 19971027 NO 1997-4508 19970929  
 US 6303141 B1 20011016 US 1999-407348 19990929  
 PRIORITY APPLN. INFO.: DE 1995-19512181 A 19950331  
 WO 1996-EP1402 W 19960329  
 US 1997-930684 B1 19970930

AB The title system consists of a solvent-permeable backing foil, a reservoir, a microporous or semipermeable membrane, an adhesive layer, and possibly a removable covering foil. In an example, the angiotensin-converting enzyme inhibitor trandolapril, dissolved in EtOH, was used in a system composed of a microporous membrane (28% ethylene vinyl acetate) and a skin-adhesive layer. Release studies showed that the delivery of the drug remained constant during 20 days, whereas that from a standard system (silicone membrane) decreased greatly with time.

IC ICM A61L015-44  
 ICS A61K031-40; A61K031-55; A61K031-66  
 CC 63-7 (Pharmaceuticals)

L257 ANSWER 20 OF 43 HCAPLUS COPYRIGHT 2006 ACS on STN

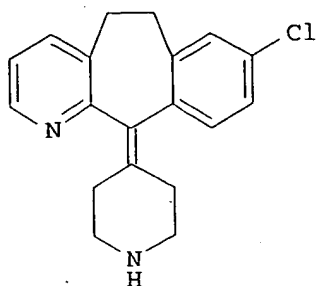
ACCESSION NUMBER: 1996:425445 HCAPLUS  
 DOCUMENT NUMBER: 125:67808  
 TITLE: Transdermal dosage system containing active loratadine metabolite  
 INVENTOR(S): Klokke, Karin; Fischer, Wilfried  
 PATENT ASSIGNEE(S): Hexal Pharma GmbH, Germany  
 SOURCE: Ger. Offen., 3 pp.  
 CODEN: GWXXBX  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4442999	A1	19960605	DE 1994-4442999	19941202
ZA 9510234	A	19960902	ZA 1995-10234	19951201
WO 9616641	A1	19960606	WO 1995-EP4761	19951204
W: AU, CA, CZ, FI, JP, NO, PL, SK, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9643015	A1	19960619	AU 1996-43015	19951204
EP 794770	A1	19970917	EP 1995-941659	19951204
EP 794770	B1	20010307		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
AT 199496	E	20010315	AT 1995-941659	19951204
ES 2156220	T3	20010616	ES 1995-941659	19951204
PT 794770	T	20010830	PT 1995-941659	19951204
US 6165498	A	20001226	US 1998-849206	19980323
US 6395297	B1	20020528	US 2000-572771	20000517
GR 3035860	T3	20010831	GR 2001-400711	20010515
PRIORITY APPLN. INFO.:			DE 1994-4442999	A 19941202
			WO 1995-EP4761	W 19951204

US 1998-849206

A1 19980323

GI



I

AB A loratadine metabolite (I) is provided which has antihistaminic activity when administered systemically from a transdermal plaster. Thus, a 2% solution of I in Duro-Tak 1753 adhesive was spread on a siliconized film to a d. of 100 g/m<sup>2</sup>, dried, laminated with a transparent polypropylene or polyester film, and cut into plasters 100-40 cm<sup>2</sup> in size.

IC ICM A61K031-445

CC 63-6 (Pharmaceuticals)

L257 ANSWER 21 OF 43 MEDLINE on STN  
ACCESSION NUMBER: 94123415 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 8293538  
TITLE: Mouse skin papilloma formation by chronic dermal application of 7,12-dimethylbenz[a]anthracene is not reduced by diet restriction.  
AUTHOR: Fischer W H; Lutz W K  
CORPORATE SOURCE: Institute of Toxicology, Swiss Federal Institute of Technology, ETH.  
SOURCE: Carcinogenesis, (1994 Jan) Vol. 15, No. 1, pp. 129-31. Journal code: 8008055. ISSN: 0143-3334.  
PUB. COUNTRY: ENGLAND: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199402  
ENTRY DATE: Entered STN: 14 Mar 1994  
Last Updated on STN: 14 Mar 1994  
Entered Medline: 25 Feb 1994

## ABSTRACT:

Diet restriction has repeatedly been shown to reduce the incidence of spontaneous and chemically induced tumors in rodents. However, no conclusive data are available to show whether carcinogenesis by chronic exposure to a genotoxic agent can also be retarded. In this study, diet restriction to 70% was investigated for a protective effect on the formation of skin papilloma in male NMRI mice treated twice weekly with 20 nmol 7,12-dimethylbenz[a]anthracene (DMBA). Rather surprisingly, no protection was seen. Both time of onset of papilloma formation (13 weeks in both groups) and time of 50% cumulative incidence (t<sub>50</sub>; 17.5 and 18 weeks) were similar in the unrestricted and the restricted group. In contrast, a clearly protective effect was found in mice initiated with 100 nmol DMBA and promoted twice weekly with 2.5 nmol 12-O-tetradecanoylphorbol-13-acetate: the onset of papilloma formation

increased from 7 to 11.5 weeks, the t50 was shifted from 8.5 to 19 weeks. Diet restriction, therefore, was not protective under conditions of chronic exposure to a genotoxic carcinogen. It cannot be considered a universal measure of cancer prevention.

CONTROLLED TERM: Check Tags: Male  
\*9,10-Dimethyl-1,2-benzanthracene  
9,10-Dimethyl-1,2-benzanthracene: AD, administration & dosage  
Administration, Cutaneous  
Animals  
Body Weight: DE, drug effects  
\*Diet, Reducing  
Dietary Carbohydrates: AD, administration & dosage  
Disease Models, Animal  
Mice  
Mice, Inbred Strains  
\*Papilloma: CI, chemically induced  
Papilloma: DH, diet therapy  
\*Papilloma: PC, prevention & control  
\*Skin Neoplasms: CI, chemically induced  
Skin Neoplasms: DH, diet therapy  
\*Skin Neoplasms: PC, prevention & control  
Time Factors  
CAS REGISTRY NO.: 57-97-6 (9,10-Dimethyl-1,2-benzanthracene)  
CHEMICAL NAME: 0 (Dietary Carbohydrates)

L257 ANSWER 22 OF 43 MEDLINE on STN  
ACCESSION NUMBER: 92319833 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 1620734  
TITLE: Comparative pharmacological investigations of Allium ursinum and Allium sativum.  
AUTHOR: Sendl A; Elbl G; Steinke B; Redl K; Breu W; Wagner H  
CORPORATE SOURCE: Institute of Pharmaceutical Biology, University of Munich, Federal Republic of Germany.  
SOURCE: Planta medica, (1992 Feb) Vol. 58, No. 1, pp. 1-7.  
Journal code: 0066751. ISSN: 0032-0943.  
PUB. COUNTRY: GERMANY: Germany, Federal Republic of  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199208  
ENTRY DATE: Entered STN: 15 Aug 1992  
Last Updated on STN: 15 Aug 1992  
Entered Medline: 4 Aug 1992

ABSTRACT:  
Extracts of wild garlic (Allium ursinum) and garlic (A. sativum) with defined chemical compositions were investigated for their in vitro inhibitory potential on 5-lipoxygenase (LO), cyclooxygenase (CO), thrombocyte aggregation (TA), and angiotensin I-converting enzyme (ACE). The inhibition rates as IC50 values of both extracts for 5-LO, CO, and TA showed a good correlation with the %-content of the major S-containing compounds (thiosulfinates and ajoenes) of the various extracts. In the 5-LO and CO test the garlic extracts are slightly superior to the wild garlic extracts whereas, in the TA test, no differences could be found. In the ACE test the water extract of the leaves of wild garlic containing glutamyl-peptides showed the highest inhibitory activity followed by that of the garlic leaf and the bulbs of both drugs. The comparative studies underline the usefulness of wild garlic as a substitute of garlic.

CONTROLLED TERM: \*Allium  
Allium: CH, chemistry

**Angiotensin-Converting Enzyme Inhibitors: PD,  
pharmacology**

**Animals**

Blood Platelets: DE, drug effects

Comparative Study

Cyclooxygenase Inhibitors: PD, pharmacology

**\*Garlic**

Garlic: CH, chemistry

**Humans**

Lipoxygenase Inhibitors: PD, pharmacology

**\*Plant Extracts: PD, pharmacology**

**\*Plants, Medicinal**

Species Specificity

CHEMICAL NAME: 0 (Angiotensin-Converting Enzyme Inhibitors); 0  
(Cyclooxygenase Inhibitors); 0 (Lipoxygenase Inhibitors); 0  
(Plant Extracts)

L257 ANSWER 23 OF 43 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights  
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ACCESSION NUMBER: 2003440622 EMBASE

TITLE: Third meeting on Novel Adjuvants Currently in or Close to  
Clinical Testing World Health Organization - Organisation  
Mondiale de la Sante, Fondation Merieux, Annecy, France,  
7-9 January 2002.

AUTHOR: Engers H.; Kieny M.P.; Malhotra P.; Pink J.R.; Davies G.;  
Kensil C.R.; Jeannin P.; Aubry J.-P.; Goetsch L.; Delneste  
Y.; Bonnefoy J.-Y.; Revets H.; De Baetselier P.; Steward  
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**Kramer K.J.**; Hashimoto A.; Nishimura T.; Vine B.;  
Chang S.; Ganne V.; Van Nest G.; Perlaza B.L.; Hurtado S.;  
Gustavo Q.; Arevalo-Herrera M.; Druilhe P. Pierre; Herrera  
S.; Doolan D.L.; Sedegah M.; et al.

CORPORATE SOURCE: M.P. Kieny, World Health Organization/IVR, Avenue Appia 20,  
CH-1211, Geneva 27, Switzerland. Kienym@who.int

SOURCE: Vaccine, (2003) Vol. 21, No. 25-26, pp. 3503-3524. .

ISSN: 0264-410X CODEN: VACCDE

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Conference Article

FILE SEGMENT: 004 Microbiology  
026 Immunology, Serology and Transplantation  
037 Drug Literature Index  
038 Adverse Reactions Titles  
039 Pharmacy

LANGUAGE: English

ENTRY DATE: Entered STN: 1 Dec 2003

Last Updated on STN: 1 Dec 2003

CONTROLLED TERM: Medical Descriptors:  
drug screening  
world health organization  
immunostimulation  
drug delivery system  
drug formulation  
drug safety  
drug effect  
drug efficacy  
low drug dose  
drug dose regimen  
drug mechanism  
drug activity  
drug antigenicity  
drug tolerability  
immunogenicity  
immunoreactivity  
immunomodulation  
humoral immunity  
cellular immunity  
cytokine production  
autoimmunity  
in vivo study  
in vitro study  
cell activation  
cell maturation  
dendritic cell  
spleen cell  
Langerhans cell  
experimental mouse  
cancer immunotherapy  
cancer prevention  
infection prevention  
immunosuppressive treatment  
patch test  
phase 1 clinical trial  
pain: SI, side effect  
Human immunodeficiency virus infection: DT, drug therapy  
Human immunodeficiency virus infection: PC, prevention  
malaria: DT, drug therapy  
malaria: PC, prevention  
melanoma: DT, drug therapy  
melanoma: PC, prevention  
Streptococcus infection: DT, drug therapy  
Streptococcus infection: PC, prevention  
influenza: DT, drug therapy  
influenza: PC, prevention  
measles: DT, drug therapy  
measles: PC, prevention  
traveller diarrhea: DT, drug therapy  
traveller diarrhea: PC, prevention  
hepatitis C: DT, drug therapy  
hepatitis C: PC, prevention  
leishmaniasis: DT, drug therapy  
leishmaniasis: PC, prevention  
Plasmodium falciparum  
Plasmodium vivax  
Plasmodium cynomolgi  
Macaca  
rhesus monkey

human  
nonhuman  
clinical trial  
conference paper  
priority journal

## CONTROLLED TERM:

## Drug Descriptors:

\*immunological adjuvant: AE, adverse drug reaction  
\*immunological adjuvant: CT, clinical trial  
\*immunological adjuvant: CB, drug combination  
\*immunological adjuvant: DV, drug development  
\*immunological adjuvant: DT, drug therapy  
\*immunological adjuvant: PR, pharmaceuticals  
\*immunological adjuvant: PK, pharmacokinetics  
\*immunological adjuvant: PD, pharmacology  
\*immunological adjuvant: IM, intramuscular drug  
administration  
\*immunological adjuvant: NA, intranasal drug administration  
\*immunological adjuvant: IV, intravenous drug  
administration  
\*immunological adjuvant: PO, oral drug administration  
\*immunological adjuvant: PA, parenteral drug administration  
\*immunological adjuvant: TP, topical drug administration  
\*immunological adjuvant: TD, transdermal drug  
administration

vaccine: AE, adverse drug reaction  
vaccine: CT, clinical trial  
vaccine: CB, drug combination  
vaccine: DV, drug development  
vaccine: DT, drug therapy  
vaccine: PR, pharmaceuticals  
vaccine: PK, pharmacokinetics  
vaccine: PD, pharmacology  
vaccine: IM, intramuscular drug administration  
vaccine: NA, intranasal drug administration  
vaccine: IV, intravenous drug administration  
vaccine: PO, oral drug administration  
vaccine: PA, parenteral drug administration  
vaccine: TP, topical drug administration

## vaccine: TD, transdermal drug administration

om 174: AE, adverse drug reaction  
om 174: CT, clinical trial  
om 174: DV, drug development  
om 174: PR, pharmaceuticals  
om 174: PD, pharmacology  
om 174: IM, intramuscular drug administration  
om 174: IV, intravenous drug administration  
om triacyl: DV, drug development  
om triacyl: PR, pharmaceuticals  
om triacyl: PD, pharmacology  
omp a: PR, pharmaceuticals  
omp a: PD, pharmacology  
lipoprotein 1: PR, pharmaceuticals  
lipoprotein 1: PD, pharmacology  
escheriagen: CT, clinical trial  
escheriagen: CB, drug combination  
escheriagen: DT, drug therapy  
escheriagen: PD, pharmacology  
qs 21: DV, drug development  
qs 21: DT, drug therapy  
qs 21: PR, pharmaceuticals

qs 21: PD, pharmacology  
 DNA vaccine: DT, drug therapy  
 DNA vaccine: PR, pharmaceuticals  
 DNA vaccine: PK, pharmacokinetics  
 DNA vaccine: PD, pharmacology  
 influenza vaccine: CT, clinical trial  
 influenza vaccine: CB, drug combination  
 influenza vaccine: DT, drug therapy  
 influenza vaccine: PR, pharmaceuticals  
 influenza vaccine: PD, pharmacology  
 virosome: PR, pharmaceuticals  
 virosome: PD, pharmacology  
 ISCOM: DV, drug development  
 ISCOM: PD, pharmacology  
 ISCOM: NA, intranasal drug administration  
 ISCOM: PA, parenteral drug administration  
 saponin: PR, pharmaceuticals  
 cholesterol: PR, pharmaceuticals  
 phospholipid: PR, pharmaceuticals  
 antigen: PR, pharmaceuticals  
 microsphere: PR, pharmaceuticals  
 polyglactin: PR, pharmaceuticals  
 polyglactin: PD, pharmacology  
 Human immunodeficiency virus vaccine: DT, drug therapy  
 Human immunodeficiency virus vaccine: PR, pharmaceuticals  
 Human immunodeficiency virus vaccine: PK, pharmacokinetics  
 Human immunodeficiency virus vaccine: PD, pharmacology  
 malaria vaccine: CB, drug combination  
 malaria vaccine: DV, drug development  
 malaria vaccine: PR, pharmaceuticals  
 malaria vaccine: PD, pharmacology  
 rt s: CB, drug combination  
 rt s: DV, drug development  
 rt s: PR, pharmaceuticals  
 rt s: PD, pharmacology  
 sbas 2: CB, drug combination  
 sbas 2: DV, drug development  
 sbas 2: PR, pharmaceuticals  
 sbas 2: PD, pharmacology  
 merozoite surface protein 1: DV, drug development  
 merozoite surface protein 1: PR, pharmaceuticals  
 merozoite surface protein 1: PD, pharmacology  
 n acetylmuramylalanyl dextro isoglutaminylalanyl  
 dipalmitoylphosphatidylethanolamine: PR, pharmaceuticals  
 n acetylmuramylalanyl dextro isoglutaminylalanyl  
 dipalmitoylphosphatidylethanolamine: PD, pharmacology  
 B7 antigen: EC, endogenous compound  
 CD86 antigen: EC, endogenous compound  
 granulocyte macrophage colony stimulating factor: EC,  
 endogenous compound  
 interleukin 4: EC, endogenous compound  
 major histocompatibility antigen class 1: EC, endogenous  
 compound  
 unindexed drug  
 unclassified drug  
 rts s  
 aso2a  
 nasal flu  
 inflexal v

CAS REGISTRY NO.: (qs 21) 141256-04-4; (saponin) 8047-15-2; (cholesterol)

CHEMICAL NAME: 57-88-5; (polyglactin) 26780-50-7, 34346-01-5; (n  
acetylmuramylalanyl dextro isoglutaminylalanyl  
dipalmitoylphosphatidylethanolamine) 83461-56-7  
(1) Rts s; (2) Sbas 2; (3) Aso2a; Escheriagen; ISCOM; Nasal  
flu; Inflexal v; Fluarix; Mf 59  
COMPANY NAME: (3) Glaxo SmithKline; Antigenics (United States); OM  
(Switzerland)

L257 ANSWER 24 OF 43 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights  
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ACCESSION NUMBER: 88091120 EMBASE  
DOCUMENT NUMBER: 1988091120  
TITLE: Development of a novel transdermal therapeutic system for  
bupranolol.  
AUTHOR: Cordes G.; Fischer W.; Legler U.; Wolff H.M.  
SOURCE: Therapeutic Research, (1988) Vol. 8, No. 1, pp. 139-154. .  
ISSN: 0289-8020 CODEN: THREEL  
COUNTRY: Japan  
DOCUMENT TYPE: Journal  
FILE SEGMENT: 037 Drug Literature Index  
018 Cardiovascular Diseases and Cardiovascular Surgery  
030 Pharmacology  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ENTRY DATE: Entered STN: 11 Dec 1991  
Last Updated on STN: 11 Dec 1991

ABSTRACT: Beta-adrenoceptor blocking drugs now occupy an important place in the treatment of angina pectoris, hypertension and other cardiovascular diseases. Patients often receive  $\beta$ -blocking drugs for many years or even for the rest of their lives. The transdermal route of application offers considerable advantages especially for treatment of chronic diseases. Whereas multidose oral application often leads to unwanted fluctuations in plasma levels, transdermal application allows plasma levels to be kept constant over the application period. For drugs undergoing extensive first pass metabolism after oral application, dosage may be reduced under transdermal treatment. The dermal application of a  $\beta$ -blocking formulation could result in a considerable benefit for the patient because an easy way of application, together with a low amount of drug necessary, could be achieved, if one succeeded in the development of a transdermal therapeutic system. My presentation will describe the substance itself, absorption experiments, pharmacodynamic, pharmacokinetic, and clinical investigations during the development of a transdermal system for bupranolol a highly potent  $\beta$ -blocking agent. Let me summarize the pharmacologic, pharmacokinetic and clinical studies: - bupranolol base is a well suited  $\beta$ -blocker for TTS development because of its high receptor affinity and good skin penetration ability - the bioavailability after oral administration is low (less than 10%) - pharmacodynamic investigation in animals as well as in humans show that the TTS controls the drug release similar to a long term infusion - the first, only preliminary clinical results, obtained in a dose finding study showed a dose depending effect on BP, HR and double product, thus indicating an antihypertensive action.

CONTROLLED TERM: Medical Descriptors:  
\*hemodynamics  
\*hypertension: DT, drug therapy  
\*pharmacodynamics  
\*pharmacokinetics  
\*transdermal drug administration  
dose response  
clinical article

human experiment  
animal experiment  
human  
nonhuman  
normal value  
intradermal drug administration  
Drug Descriptors:  
\*bupranolol: PD, pharmacology  
\*bupranolol: DT, drug therapy  
\*bupranolol: PK, pharmacokinetics  
\*bupranolol: AD, drug administration  
CAS REGISTRY NO.: (bupranolol) 14556-46-8, 15148-80-8  
COMPANY NAME: Pharma schwarz

L257 ANSWER 25 OF 43 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 87086277 EMBASE  
DOCUMENT NUMBER: 1987086277  
TITLE: Inhibition of thrombocyte aggregation by oral motapizone and other drugs.  
AUTHOR: Schulz V.; Fischer W.; Hansell U.; Zietsch V.  
CORPORATE SOURCE: University Medical Clinic I, D-5000 Koln 41, Germany  
SOURCE: European Journal of Clinical Pharmacology, (1986) Vol. 31, No. 4, pp. 411-414. .  
CODEN: EJCPAS  
COUNTRY: Germany  
DOCUMENT TYPE: Journal  
FILE SEGMENT: 037 Drug Literature Index  
030 Pharmacology  
018 Cardiovascular Diseases and Cardiovascular Surgery  
025 Hematology  
LANGUAGE: English  
ENTRY DATE: Entered STN: 11 Dec 1991  
Last Updated on STN: 11 Dec 1991

ABSTRACT: Ten healthy subjects took single oral doses of placebo,  $8.8 \pm 1.8$  mg motapizone,  $40 \pm 13$  mg captopril, 25 mg dihydralazine, 20 mg nifedipine and  $4.5 \pm 1.1$  mg prazosin in random order, and, as the last preparation 500 mg acetylsalicylic acid. Thrombocyte aggregation induced 'ex-vivo' with collagen, ADP and adrenaline was measured before and after 60 min. Immediately before each dose, the 'threshold concentration' of each agent was determined in each subject, i.e. the concentration producing about 90% of maximal aggregation. After the preparation had been taken, aggregation was induced with 1-, 2- and 4-times the threshold concentration. Both motapizone and acetylsalicylic acid caused marked inhibition of aggregation at up to 4-times the threshold concentration; the dose ratio was about 1:50. Motapizone produced greater inhibition of the aggregation induced by ADP and acetylsalicylic acid than of that due to collagen. The inhibitory actions after captopril, dihydralazine, nifedipine and prazosin were weak and did not significantly differ from placebo.

CONTROLLED TERM: Medical Descriptors:  
\*drug efficacy  
\*human  
\*thrombocyte aggregation  
drug comparison  
oral drug administration  
priority journal  
normal human  
blood and hemopoietic system  
human experiment

## Drug Descriptors:

\*acetylsalicylic acid

\*captopril

\*hydralazine

\*motapizone

\*nifedipine

placebo

\*dihydralazine

\*methyalsalicylic acid

\*prazosin

unclassified drug

CAS REGISTRY NO.: (acetylsalicylic acid) 493-53-8, 50-78-2, 53663-74-4,  
 53664-49-6, 63781-77-1; (captopril) 62571-86-2;  
 (hydralazine) 304-20-1, 86-54-4; (motapizone) 90697-57-7;  
 (nifedipine) 21829-25-4; (dihydralazine) 484-23-1;  
 (prazosin) 19216-56-9, 19237-84-4

L257 ANSWER 26 OF 43 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on  
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ACCESSION NUMBER: 2003:493293 BIOSIS

DOCUMENT NUMBER: PREV200300495254

TITLE: Patch for transdermal application for pergolid.

AUTHOR(S): **Fischer, Wilfried** [Inventor, Reprint Author];  
**Sendl-Lang, Anna** [Inventor]; Zeh-Herwerth, Dagmar  
 [Inventor]

CORPORATE SOURCE: Holzkirchen, Germany

ASSIGNEE: Hexal AG, Holzkirchen, Germany

PATENT INFORMATION: US 6623752 20030923

SOURCE: Official Gazette of the United States Patent and Trademark  
 Office Patents, (Sep 23 2003) Vol. 1274, No. 4.  
<http://www.uspto.gov/web/menu/patdata.html>. e-file.  
 ISSN: 0098-1133 (ISSN print).

DOCUMENT TYPE: Patent

LANGUAGE: English

ENTRY DATE: Entered STN: 22 Oct 2003

Last Updated on STN: 22 Oct 2003

ABSTRACT: The invention relates to a patch for transdermal application of  
 pergolid and its pharmaceutically acceptable salts.

NAT. PATENT. CLASSIF.: 424449000

CONCEPT CODE: Pathology - Therapy 12512  
 Pharmacology - General 22002

INDEX TERMS: Major Concepts

Equipment Apparatus Devices and Instrumentation;  
 Pharmacy (Allied Medical Sciences)

INDEX TERMS: Methods &amp; Equipment

pergolid transdermal application patch: drug delivery  
 device

L257 ANSWER 27 OF 43 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on  
 STN

ACCESSION NUMBER: 2002:358640 BIOSIS

DOCUMENT NUMBER: PREV200200358640

TITLE: Transdermal preparation contacting a loratidine metabolite  
 with antihistaminic activity.

AUTHOR(S): **Klokke, Karin** [Inventor, Reprint author];  
**Fischer, Wilfried** [Inventor]; Bracher, Daniel  
 [Inventor]

CORPORATE SOURCE: Lenggries, Germany

ASSIGNEE: Hexal AG, Holzkirchen, Germany

PATENT INFORMATION: US 6395297 20020528

SOURCE: Official Gazette of the United States Patent and Trademark  
Office Patents, (May 28, 2002) Vol. 1258, No. 4.  
<http://www.uspto.gov/web/menu/patdata.html>. e-file.  
CODEN: OGUPE7. ISSN: 0098-1133.

DOCUMENT TYPE: Patent  
LANGUAGE: English  
ENTRY DATE: Entered STN: 26 Jun 2002  
Last Updated on STN: 26 Jun 2002

ABSTRACT: A transdermal patch contains an active loratidine metabolite contained with polyacrylate polymer matrix. The transdermal patch provides pharmaceutically useful transdermal flux rates over time.

NAT. PATENT. CLASSIF.: 424448000

CONCEPT CODE: Pharmacology - General 22002  
Pharmacology - Immunological processes and allergy 22018

INDEX TERMS: Major Concepts  
Pharmacology

INDEX TERMS: Chemicals & Biochemicals  
loratidine metabolite: antihistamine-drug,  
immunologic-drug, transdermal administration

INDEX TERMS: Methods & Equipment  
loratidine metabolite preparation: synthetic method

L257 ANSWER 28 OF 43 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on  
STN

ACCESSION NUMBER: 2001:575756 BIOSIS  
DOCUMENT NUMBER: PREV200100575756  
TITLE: Transdermally administrable medicament with ACE inhibitors.  
AUTHOR(S): Fischer, Wilfried [Inventor, Reprint author];  
Klokkers, Karin [Inventor]; Sendl-Lang,  
Anna [Inventor]

CORPORATE SOURCE: Holzkirchen, Germany  
ASSIGNEE: Hexal AG, Germany

PATENT INFORMATION: US 6303141 20011016

SOURCE: Official Gazette of the United States Patent and Trademark  
Office Patents, (Oct. 16, 2001) Vol. 1251, No. 3. e-file.  
CODEN: OGUPE7. ISSN: 0098-1133.

DOCUMENT TYPE: Patent  
LANGUAGE: English  
ENTRY DATE: Entered STN: 12 Dec 2001  
Last Updated on STN: 25 Feb 2002

ABSTRACT: The invention relates to a transdermal system containing at least one angiotensin-converting enzyme inhibitor.

NAT. PATENT. CLASSIF.: 424449000

CONCEPT CODE: General biology - Miscellaneous 00532

INDEX TERMS: Major Concepts  
Pharmacology

INDEX TERMS: Chemicals & Biochemicals  
transdermally administrable medicament:  
angiotensin-converting enzyme inhibitor-drug

L257 ANSWER 29 OF 43 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on  
STN

ACCESSION NUMBER: 2001:459042 BIOSIS  
DOCUMENT NUMBER: PREV200100459042  
TITLE: Controlled-release pharmaceutical preparation comprising an  
ACE inhibitor as active ingredient.

AUTHOR(S): Fischer, Wilfried [Inventor, Reprint author];  
Klokkers, Karin [Inventor]; Oppelt, Renate  
[Inventor]

CORPORATE SOURCE: Holzkirchen, Germany

ASSIGNEE: Hexal AG, Holzkirchen, Germany  
PATENT INFORMATION: US 6267990 20010731  
SOURCE: Official Gazette of the United States Patent and Trademark  
Office Patents, (July 31, 2001) Vol. 1248, No. 5. e-file.  
CODEN: OGUPE7. ISSN: 0098-1133.  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
ENTRY DATE: Entered STN: 26 Sep 2001  
Last Updated on STN: 22 Feb 2002  
ABSTRACT: The invention relates to a pharmaceutical preparation which comprises  
or consists of the following components: (i) an initial dose of active  
ingredient, which is provided by the active ingredient together with optional  
excipients, (ii) a first delayed-release type of pellet, in which the active  
ingredient and optional excipients are covered with a coating, and (iii) a  
second delayed-release type of pellet, in which the active ingredient and  
optional excipients are again covered with a coating, wherein the active  
ingredient is an ACE inhibitor, and wherein the amounts of the coatings  
according to (ii) and (iii) are present in a ratio, based on weight, within the  
range of from 1:2 to 1:7.  
NAT. PATENT. CLASSIF.: 424490000  
CONCEPT CODE: General biology - Miscellaneous 00532  
INDEX TERMS: Major Concepts  
Pharmacology  
INDEX TERMS: Chemicals & Biochemicals  
angiotensin-converting enzyme inhibitor controlled  
release pharmaceutical preparation: angiotensin-  
converting enzyme inhibitor-drug

L257 ANSWER 30 OF 43 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on  
STN

ACCESSION NUMBER: 2001:404477 BIOSIS  
DOCUMENT NUMBER: PREV200100404477  
TITLE: Pharmaceutical antacid.  
AUTHOR(S): **Klokkers, Karin** [Inventor, Reprint author];  
**Kutschera, Marion** [Inventor]; **Fischer, Wilfried**  
[Inventor]  
CORPORATE SOURCE: Holzkirchen, Germany  
ASSIGNEE: Hexal AG, Holzkirchen, Germany  
PATENT INFORMATION: US 6248758 20010619  
SOURCE: Official Gazette of the United States Patent and Trademark  
Office Patents, (June 19, 2001) Vol. 1247, No. 3. e-file.  
CODEN: OGUPE7. ISSN: 0098-1133.  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
ENTRY DATE: Entered STN: 22 Aug 2001  
Last Updated on STN: 22 Feb 2002

ABSTRACT: A pharmaceutical formulation comprising a benzimidazole derivative as  
active ingredient, and as excipients, at least one cyclodextrin and at least  
one amino acid.

NAT. PATENT. CLASSIF.: 514338000  
CONCEPT CODE: General biology - Miscellaneous 00532  
INDEX TERMS: Major Concepts  
Gastroenterology (Human Medicine, Medical Sciences);  
Pharmacology  
INDEX TERMS: Chemicals & Biochemicals  
benzimidazole: gastrointestinal-drug, antacid,  
derivative  
REGISTRY NUMBER: 51-17-2 (benzimidazole)

L257 ANSWER 31 OF 43 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on

STN

ACCESSION NUMBER: 2001:295324 BIOSIS  
DOCUMENT NUMBER: PREV200100295324  
TITLE: Transdermal preparation containing a loratidine metabolite with antihistaminic activity.  
AUTHOR(S): **Klokke**, Karin [Inventor, Reprint author];  
**Fischer, Wilfried** [Inventor]; Bracher, Daniel [Inventor]  
CORPORATE SOURCE: Lenggries, Germany  
ASSIGNEE: Hexal AG, Holzkirchen, Germany  
PATENT INFORMATION: US 6165498 20001226  
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Dec. 26, 2000) Vol. 1241, No. 4. e-file.  
CODEN: OGUPE7. ISSN: 0098-1133.  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
ENTRY DATE: Entered STN: 20 Jun 2001  
Last Updated on STN: 19 Feb 2002  
ABSTRACT: A transdermal patch contains an active loratidine metabolite contained with a polyacrylate polymer matrix. The transdermal patch provides pharmaceutically useful transdermal flux rates over time.  
NAT. PATENT. CLASSIF.: 424448000  
CONCEPT CODE: General biology - Miscellaneous 00532  
INDEX TERMS: Major Concepts  
Equipment, Apparatus, Devices and Instrumentation;  
Methods and Techniques; Pharmacology  
INDEX TERMS: Chemicals & Biochemicals  
loratidine metabolite: antihistamine-drug  
INDEX TERMS: Methods & Equipment  
transdermal patch: medical supplies; transdermal patch preparation: preparation method

L257 ANSWER 32 OF 43 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2001:77708 BIOSIS  
DOCUMENT NUMBER: PREV200100077708  
TITLE: Diclofenac/gamma-cyclodextrin inclusion compounds.  
AUTHOR(S): **Fischer, Wilfried** [Inventor, Reprint author];  
**Sendl-Lang, Anna** [Inventor]  
CORPORATE SOURCE: Holzkirchen, Germany  
ASSIGNEE: Hexal AG, Holzkirchen, Germany  
PATENT INFORMATION: US 6071964 20000606  
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (June 6, 2000) Vol. 1235, No. 1. e-file.  
CODEN: OGUPE7. ISSN: 0098-1133.  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
ENTRY DATE: Entered STN: 7 Feb 2001  
Last Updated on STN: 12 Feb 2002  
ABSTRACT: The object of the present invention is an oral drug preparation containing the gamma-cyclodextrin complex of diclofenac or pharmaceutically acceptable salts thereof, especially the sodium salt prepared by known methods, and by which the gastro-intestinal irritancy of diclofenac, at the same or improved bioavailability, can be considerably decreased.  
NAT. PATENT. CLASSIF.: 514567000  
CONCEPT CODE: General biology - Miscellaneous 00532  
INDEX TERMS: Major Concepts  
Pharmacology  
INDEX TERMS: Chemicals & Biochemicals  
diclofenac/gamma-cyclodextrin complex: oral

## administration

L257 ANSWER 33 OF 43 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on  
STN

ACCESSION NUMBER: 2000:289943 BIOSIS  
DOCUMENT NUMBER: PREV200000289943  
TITLE: Transdermal system of tacrine/selegilin-plaster.  
AUTHOR(S): **Sendl-Lang, Ann** [Inventor, Reprint author];  
**Fischer, Wilfried** [Inventor]  
CORPORATE SOURCE: Holzkirchen, Germany  
ASSIGNEE: Hexal; Hexal, A.G., Munich, Germany  
PATENT INFORMATION: US 5972376 19991026  
SOURCE: Official Gazette of the United States Patent and Trademark  
Office Patents, (Oct. 26, 1999) Vol. 1227, No. 4. e-file.  
CODEN: OGUPE7. ISSN: 0098-1133.  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
ENTRY DATE: Entered STN: 6 Jul 2000  
Last Updated on STN: 7 Jan 2002  
ABSTRACT: The invention relates to a plaster for transdermal application with an  
outer covering or backing layer, a self-adhesive matrix or a reservoir and a  
removable protective liner or release layer, the matrix or the reservoir  
containing tacrine and selegiline (optionally in the form of their  
pharmaceutically compatible salts) as active substance.  
NAT. PATENT. CLASSIF.: 424449000  
CONCEPT CODE: General biology - Miscellaneous 00532  
INDEX TERMS: Major Concepts  
Dental and Oral System (Ingestion and Assimilation);  
Pharmacology  
INDEX TERMS: Chemicals & Biochemicals  
tacrine-selegilin plaster  
INDEX TERMS: Miscellaneous Descriptors  
transdermal application  
ORGANISM: Classifier  
Enterobacteriaceae 06702  
Super Taxa  
Facultatively Anaerobic Gram-Negative Rods; Eubacteria;  
Bacteria; Microorganisms  
Organism Name  
Escherichia coli  
Taxa Notes  
Bacteria, Eubacteria, Microorganisms

L257 ANSWER 34 OF 43 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on  
STN

ACCESSION NUMBER: 1999:381934 BIOSIS  
DOCUMENT NUMBER: PREV199900381934  
TITLE: Tablet or capsule having a content of stable ranitidine  
hydrochloride form 1.  
AUTHOR(S): **Fischer, Wilfried** [Inventor, Reprint author];  
**Klokke, Karin** [Inventor]  
CORPORATE SOURCE: Holzkirchen, West Germany  
ASSIGNEE: Hexal AG  
PATENT INFORMATION: US 5910320 19990608  
SOURCE: Official Gazette of the United States Patent and Trademark  
Office Patents, (Jun. 08, 1999) Vol. 1223, No. 2. print.  
CODEN: OGUPE7. ISSN: 0098-1133.  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
ENTRY DATE: Entered STN: 13 Sep 1999

Last Updated on STN: 13 Sep 1999  
NAT. PATENT. CLASSIF.: 424465000  
CONCEPT CODE: General biology - Miscellaneous 00532  
INDEX TERMS: Major Concepts  
Methods and Techniques; Pharmaceuticals (Pharmacology)  
INDEX TERMS: Chemicals & Biochemicals  
ranitidine hydrochloride: form 1 capsule, form 1 tablet  
REGISTRY NUMBER: 66357-59-3 (ranitidine hydrochloride)

L257 ANSWER 35 OF 43 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 1999:144983 BIOSIS  
DOCUMENT NUMBER: PREV199900144983  
TITLE: Sustained release tablet containing diclofenac-Na and methylhydroxypropylcellulose as a sustained release agent.  
AUTHOR(S): Fischer, W. [Inventor]; Klokke, K. [Inventor]  
CORPORATE SOURCE: Holzkirchen, Germany  
ASSIGNEE: HEXAL AG  
PATENT INFORMATION: US 5874107 19990223  
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Feb. 23, 1999) Vol. 1219, No. 4, pp. 3272. print.  
CODEN: OGUPE7. ISSN: 0098-1133.  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
ENTRY DATE: Entered STN: 13 Apr 1999  
Last Updated on STN: 13 Apr 1999

NAT. PATENT. CLASSIF.: 424464000  
CONCEPT CODE: General biology - Miscellaneous 00532  
INDEX TERMS: Major Concepts  
Biochemistry and Molecular Biophysics; Pharmacology  
INDEX TERMS: Miscellaneous Descriptors  
DICLOFENAC-NA; METHYLHYDROXYPROPYLCELLULOSE;  
PHARMACEUTICALS; SUSTAINED RELEASE TABLET

L257 ANSWER 36 OF 43 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 1999:364398 BIOSIS  
DOCUMENT NUMBER: PREV199900364398  
TITLE: Transdermal system in the form of a patch comprising a tamoxifen derivative.  
AUTHOR(S): Fischer, Wilfried [Inventor, Reprint author]; Klokke, Karin [Inventor]; Sendl-Lang, Anna [Inventor]  
CORPORATE SOURCE: Holzkirchen, West Germany  
ASSIGNEE: Hexal AG  
PATENT INFORMATION: US 5904930 19990518  
SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (5/18/1999) Vol. 1222, No. 3. print.  
CODEN: OGUPE7. ISSN: 0098-1133.  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
ENTRY DATE: Entered STN: 2 Sep 1999  
Last Updated on STN: 2 Sep 1999

NAT. PATENT. CLASSIF.: 424448000  
CONCEPT CODE: General biology - Miscellaneous 00532  
INDEX TERMS: Major Concepts  
Equipment, Apparatus, Devices and Instrumentation;  
Methods and Techniques; Pharmaceuticals (Pharmacology);

INDEX TERMS: Tumor Biology  
Diseases  
cancer: neoplastic disease  
Neoplasms (MeSH)

INDEX TERMS: Chemicals & Biochemicals  
tamoxifen: antineoplastic-drug

INDEX TERMS: Methods & Equipment  
transdermal patch technique: drug delivery method;  
transdermal patch: medical supplies

REGISTRY NUMBER: 10540-29-1 (tamoxifen)

L257 ANSWER 37 OF 43 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on  
STN

ACCESSION NUMBER: 2002:127299 BIOSIS  
DOCUMENT NUMBER: PREV200200127299  
TITLE: Active ingredients patch.  
AUTHOR(S): Fischer, W. [Inventor]; Klokkeers, K.  
[Inventor]  
CORPORATE SOURCE: Holzkirchen, Germany  
ASSIGNEE: HEXAL PHARMA GMBH  
PATENT INFORMATION: US 5830505 19981103  
SOURCE: Official Gazette of the United States Patent and Trademark  
Office Patents, (Nov. 3, 1998) Vol. 1216, No. 1, pp. 491.  
print.  
CODEN: OGUPE7. ISSN: 0098-1133.

DOCUMENT TYPE: Patent  
LANGUAGE: English  
ENTRY DATE: Entered STN: 30 Jan 2002  
Last Updated on STN: 26 Feb 2002

NAT. PATENT. CLASSIF.: 424487000

CONCEPT CODE: Biochemistry studies - General 10060  
Integumentary system - General and methods 18501  
Pharmacology - General 22002  
Pathology - Therapy 12512

INDEX TERMS: Major Concepts  
Biochemistry and Molecular Biophysics; Integumentary  
System (Chemical Coordination and Homeostasis);  
Pathology; Pharmacology

INDEX TERMS: Miscellaneous Descriptors  
CHEMICAL FORMULA; DRUG DELIVERY DEVICE; PHARMACEUTICALS

L257 ANSWER 38 OF 43 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on  
STN

ACCESSION NUMBER: 2002:85994 BIOSIS  
DOCUMENT NUMBER: PREV200200085994  
TITLE: Active ingredient patch.  
AUTHOR(S): Fischer, W. [Inventor]; Klokkeers, K.  
[Inventor]  
CORPORATE SOURCE: Holzkirchen, Germany  
ASSIGNEE: HEXAL PHARMA GMBH  
PATENT INFORMATION: US 5683711 19971104  
SOURCE: Official Gazette of the United States Patent and Trademark  
Office Patents, (Nov. 4, 1997) Vol. 1204, No. 1, pp.  
384-385. print.  
CODEN: OGUPE7. ISSN: 0098-1133.

DOCUMENT TYPE: Patent  
LANGUAGE: English  
ENTRY DATE: Entered STN: 16 Jan 2002  
Last Updated on STN: 25 Feb 2002

NAT. PATENT. CLASSIF.: 424449000

CONCEPT CODE: Integumentary system - General and methods 18501  
 Pharmacology - General 22002  
 INDEX TERMS: Major Concepts  
 Integumentary System (Chemical Coordination and Homeostasis); Pharmacology  
 INDEX TERMS: Miscellaneous Descriptors  
 DRUG DELIVERY; DRUG PATCH; PHARMACEUTICALS; TRANSDERMAL PATCH

L257 ANSWER 39 OF 43 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:83333 BIOSIS  
 DOCUMENT NUMBER: PREV200200083333  
 TITLE: Crystalline cyclodextrin complexes of ranitidine hydrochloride, process for their preparation and pharmaceutical compositions containing the same.  
 AUTHOR(S): Fischer, W. [Inventor]; Klokke, K. [Inventor]  
 CORPORATE SOURCE: Holzkirchen, Germany  
 ASSIGNEE: HEXAL PHARMA GMBH  
 PATENT INFORMATION: US 5665767 19970909  
 SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Sept. 9, 1997) Vol. 1202, No. 2, pp. 1386. print.  
 CODEN: OGUPE7. ISSN: 0098-1133.  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 ENTRY DATE: Entered STN: 16 Jan 2002  
 Last Updated on STN: 25 Feb 2002  
 NAT. PATENT. CLASSIF.: 514471000  
 CONCEPT CODE: Biochemistry studies - General 10060  
 Pharmacology - General 22002  
 Methods - Laboratory methods 01004  
 INDEX TERMS: Major Concepts  
 Biochemistry and Molecular Biophysics; Methods and Techniques; Pharmacology  
 INDEX TERMS: Miscellaneous Descriptors  
 BETA-CYCLODEXTRIN HOST SUBSTANCE; MANUFACTURING METHODS; PHARMACEUTICALS

L257 ANSWER 40 OF 43 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN  
 ACCESSION NUMBER: 1996-464638 [46] WPIX  
 DOC. NO. CPI: C1996-145829  
 TITLE: Transdermal delivery system for ACE inhibitor - contains inhibitor (opt. as pro-drug, especially ramipril or trandolapril) incorporated in polyisobutylene or butyl rubber matrix.  
 DERWENT CLASS: A96 B02 B07 P32 P34  
 INVENTOR(S): FISCHER, W; KLOKKERS, K;  
 SENDL-LANG, A; LANG, A S; FISHER, W  
 PATENT ASSIGNEE(S): (HEXA-N) HEXAL AG; (HEXA-N) HEXAL PHARMA GMBH  
 COUNTRY COUNT: 64  
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN	IPC
WO 9629999	A1	19961003	(199646)*	GE	20	A61K009-70	
RW: AT BE CH DE DK ES FI FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE							
SZ UG							
W: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU JP KE KG							

KP KR KZ LK LR LT LU LV MD MG MN MW MX NO NZ PL PT RO RU SD SE SI  
 SK TJ TT UA US UZ VN

DE 19512181 A1 19961002 (199646) 6 A61L015-44  
 AU 9654982 A 19961016 (199706) A61K009-70  
 NO 9704508 A 19971027 (199802) A61M037-00  
 EP 817622 A1 19980114 (199807) GE A61K009-70  
 R: AT CH DE DK ES GB LI LT LU LV NL PT SE SI  
 ZA 9602592 A 19971231 (199807) 14 A61K000-00  
 CZ 9703028 A3 19980218 (199813) A61K009-70  
 SK 9701258 A3 19980204 (199818) A61K009-70  
 MX 9707507 A1 19971101 (199902) A61K009-70  
 AU 700418 B 19990107 (199913) A61K009-70  
 HU 9801989 A2 19990301 (199916) A61K009-70  
 JP 11502827 W 19990309 (199920) 15 A61K009-70  
 BR 9607872 A 19991130 (200014) A61K009-70  
 NZ 306429 A 20000728 (200043) A61K038-55  
 CZ 287373 B6 20001115 (200064) A61K009-70  
 US 6303141 B1 20011016 (200164) A61K009-70  
 EP 817622 B1 20011128 (200201) GE A61K009-70  
 R: AT CH DE DK ES GB LI LT LU LV NL PT SE SI  
 DE 59608323 G 20020110 (200206) A61K009-70  
 CN 1179712 A 19980422 (200222) A61K009-70  
 ES 2167558 T3 20020516 (200239) A61K009-70  
 DE 19512181 C2 20031106 (200374) A61L015-44

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9629999	A1	WO 1996-EP1402	19960329
DE 19512181	A1	DE 1995-1012181	19950331
AU 9654982	A	AU 1996-54982	19960329
NO 9704508	A	WO 1996-EP1402	19960329
		NO 1997-4508	19970929
EP 817622	A1	EP 1996-911973	19960329
		WO 1996-EP1402	19960329
ZA 9602592	A	ZA 1996-2592	19960401
CZ 9703028	A3	WO 1996-EP1402	19960329
		CZ 1997-3028	19960329
SK 9701258	A3	WO 1996-EP1402	19960329
		SK 1997-1258	19960329
MX 9707507	A1	MX 1997-7507	19970930
AU 700418	B	AU 1996-54982	19960329
HU 9801989	A2	WO 1996-EP1402	19960329
		HU 1998-1989	19960329
JP 11502827	W	JP 1996-528948	19960329
		WO 1996-EP1402	19960329
BR 9607872	A	BR 1996-7872	19960329
		WO 1996-EP1402	19960329
NZ 306429	A	NZ 1996-306429	19960329
		WO 1996-EP1402	19960329
CZ 287373	B6	WO 1996-EP1402	19960329
		CZ 1997-3028	19960329
US 6303141	B1 Cont of Cont of	WO 1996-EP1402	19960329
		US 1997-930684	19970930
		US 1999-407348	19990929
EP 817622	B1	EP 1996-911973	19960329
		WO 1996-EP1402	19960329
DE 59608323	G	DE 1996-508323	19960329
		EP 1996-911973	19960329

CN 1179712	A	WO 1996-EP1402	19960329
ES 2167558	T3	CN 1996-192839	19960329
DE 19512181	C2	EP 1996-911973	19960329
		DE 1995-1012181	19950331

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9654982	A Based on	WO 9629999
EP 817622	A1 Based on	WO 9629999
CZ 9703028	A3 Based on	WO 9629999
AU 700418	B Previous Publ. Based on	AU 9654982
		WO 9629999
HU 9801989	A2 Based on	WO 9629999
JP 11502827	W Based on	WO 9629999
BR 9607872	A Based on	WO 9629999
NZ 306429	A Based on	WO 9629999
CZ 287373	B6 Previous Publ. Based on	CZ 9703028
		WO 9629999
EP 817622	B1 Based on	WO 9629999
DE 59608323	G Based on	EP 817622
	Based on	WO 9629999
ES 2167558	T3 Based on	EP 817622

PRIORITY APPLN. INFO: DE 1995-19512181 19950331  
 REFERENCE PATENTS: EP 425837; EP 439430; WO 9323019  
 INT. PATENT CLASSIF.:

MAIN: A61K000-00; A61K009-70; A61K038-55; A61L015-44;  
 A61M037-00

SECONDARY: A61F013-00; A61K009-14; A61K031-40; A61K031-55;  
 A61K031-66; A61K045-00; A61M031-40; A61P009-12

## BASIC ABSTRACT:

WO 9629999 A UPAB: 20011129

A transdermal delivery system containing a polyisobutylene or butyl rubber matrix incorporating at least one angiotensin converting enzyme (ACE) inhibitor is claimed.

Pref. ACE inhibitor is ramipril ortrandolapril, as such or as a pro-drug, salt, etc. The system may also contain a permeation promoter, especially Eutanol G.

USE - The system is used for the continuous admin. of ACE inhibitors over an extended period. The ACE inhibitor can be present pref. in an amount of at least 5 weight%, especially 10-20 weight%, based on the matrix.

ADVANTAGE - The system is superior to transdermal systems known from WO 9323019, EP 4393430 and EP 468875. The ACE inhibitor release is continuous for up to 1 week giving therapeutically effective plasma levels. E.g. release can be 0.01-0.1 mg/sq. cm./24 hrs., especially 0.025-0.05 mg/sq. cm./24 hrs, giving a constant therapeutically effective trandolapril plasma concentration of above 0.5 ng/ml.

Dwg.0/1

FILE SEGMENT: CPI GMPI  
 FIELD AVAILABILITY: AB; DCN  
 MANUAL CODES: CPI: A04-G05; A04-G05A; A12-V01; B04-C02A; B04-C03B;  
 B04-C03D; B05-B01C; B06-D01; B12-M02F;  
 B12-M10A; B14-F02B1

L257 ANSWER 41 OF 43 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN  
 ACCESSION NUMBER: 1996-277455 [28] WPIX  
 DOC. NO. CPI: C1996-087998  
 TITLE: Transdermal compsn. with antihistamine activity

comprising active loratadine metabolite - is administered  
e.g. in salve or transdermal plaster, shows improved  
antihistaminic activity.

DERWENT CLASS: B02 B07 D22  
INVENTOR(S): FISCHER, W; KLOKKERS, K; BRACHER, D  
PATENT ASSIGNEE(S): (HEXA-N) HEXAL AG; (HEXA-N) HEXAL PHARMA GMBH  
COUNTRY COUNT: 27  
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN	IPC
WO 9616641	A1	19960606	(199628)*	GE	12	A61K009-70	
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE							
W: AU CA CZ FI JP NO PL SK US							
DE 4442999	A1	19960605	(199629)		4	A61K031-445	
AU 9643015	A	19960619	(199640)			A61K009-70	
ZA 9510234	A	19961129	(199702)		7	A61K000-00	
EP 794770	A1	19970917	(199742)	GE		A61K009-70	
R: AT BE CH DE DK ES FR GB GR IE IT LI LU NL PT SE							
US 6165498	A	20001226	(200103)			A61K009-70	
EP 794770	B1	20010307	(200114)	GE		A61K009-70	
R: AT BE CH DE DK ES FR GB GR IE IT LI LU NL PT SE							
DE 59509084	G	20010412	(200122)			A61K009-70	
ES 2156220	T3	20010616	(200141)			A61K009-70	
US 6395297	B1	20020528	(200243)			A61K009-70	

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9616641	A1	WO 1995-EP4761	19951204
DE 4442999	A1	DE 1994-4442999	19941202
AU 9643015	A	AU 1996-43015	19951204
ZA 9510234	A	ZA 1995-10234	19951201
EP 794770	A1	EP 1995-941659	19951204
		WO 1995-EP4761	19951204
US 6165498	A	WO 1995-EP4761	19951204
		US 1998-849206	19980323
EP 794770	B1	EP 1995-941659	19951204
		WO 1995-EP4761	19951204
DE 59509084	G	DE 1995-509084	19951204
		EP 1995-941659	19951204
		WO 1995-EP4761	19951204
ES 2156220	T3	EP 1995-941659	19951201
US 6395297	B1	WO 1995-EP4761	19951201
	Cont of	US 1998-849206	19980323
	Cont of	US 2000-572771	20000517

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9643015	A Based on	WO 9616641
EP 794770	A1 Based on	WO 9616641
US 6165498	A Based on	WO 9616641
EP 794770	B1 Based on	WO 9616641
DE 59509084	G Based on	EP 794770
	Based on	WO 9616641
ES 2156220	T3 Based on	EP 794770
US 6395297	B1 Cont of	US 6165498

PRIORITY APPLN. INFO: DE 1994-4442999 19941202  
 REFERENCE PATENTS: 2.Jnl.Ref; US 4910205  
 INT. PATENT CLASSIF.:  
 MAIN: A61K000-00; A61K009-70; A61K031-445  
 SECONDARY: A61K031-445

## BASIC ABSTRACT:

WO 9616641 A UPAB: 20020730

Pharmaceutical compsn. for systemic transdermal admin. comprises an active loratadine metabolite as active agent.

USE - The active cpd. is useful as an antihistamine. It may be administered, e.g. in a salve or a transdermal plaster.

ADVANTAGE - Loratadine is metabolised in the body. It is normally available as a solution or in tablet form. The new compsn. shows improved antihistamine effect.

Dwg.0/0

FILE SEGMENT: CPI  
 FIELD AVAILABILITY: AB; DCN  
 MANUAL CODES: CPI: B06-D13; B12-M02F; B14-L09; D09-C04B

L257 ANSWER 42 OF 43 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN  
 ACCESSION NUMBER: 1989-310850 [43] WPIX  
 DOC. NO. CPI: C1989-137549  
 TITLE: Oral pharmaceutical dosage forms with delayed release - comprising core, drug layer, opt. inner membrane, acid layer and outer membrane.  
 DERWENT CLASS: A96 B07 P33  
 INVENTOR(S): FISCHER, W; KLOKKERS-BETHKE, K; KLOKKERS, K  
 PATENT ASSIGNEE(S): (SCHW-N) SCHWARZ PHARMA AG; (SCHW-N) SCHWARZ PHARM AG  
 COUNTRY COUNT: 15  
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN	IPC
EP 338383	A	19891025	(198943)*	GE	16		
R: AT BE CH DE ES FR GB GR IT LI LU NL SE							
DE 3812799	A	19891026	(198944)				
JP 02022222	A	19900125	(199010)				
EP 338383	B1	19930324	(199312)	GE	22	A61K009-54	
R: AT BE CH DE ES FR GB GR IT LI LU NL SE							
DE 58903856	G	19930429	(199318)			A61K009-54	
ES 2054918	T3	19940816	(199434)			A61K009-54	
US 5472710	A	19951205	(199603)		14	A61K009-22	
JP 2792904	B2	19980903	(199840)		11	A61K009-56	

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 338383	A	EP 1989-106384	19890411
DE 3812799	A	DE 1988-3812799	19880416
JP 02022222	A	JP 1989-94297	19890413
EP 338383	B1	EP 1989-106384	19890411
DE 58903856	G	DE 1989-503856	19890411
		EP 1989-106384	19890411
ES 2054918	T3	EP 1989-106384	19890411
US 5472710	A	US 1989-337636	19890413
	CIP of	US 1992-956456	19921002
	Cont of	US 1994-235188	19940429

JP 2792904

B2

JP 1989-94297

19890413

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
DE 58903856	G Based on	EP 338383
ES 2054918	T3 Based on	EP 338383
JP 2792904	B2 Previous Publ.	JP 02022222

PRIORITY APPLN. INFO: DE 1988-3812799 19880416

REFERENCE PATENTS: A3...9013; EP 32562; EP 40590; EP 92060; No-SR.Pub

INT. PATENT CLASSIF.:

MAIN: A61K009-22; A61K009-54; A61K009-56

SECONDARY: A61J003-06; A61K009-24; A61K009-52

## BASIC ABSTRACT:

EP 338383 A UPAB: 19981021

Oral dosage forms comprise a core, a drug-containing layer, opt. an inner membrane, an acid layer, and an outer membrane.

ADVANTAGE - The drug is released after a lag time determined by the compsn. and thickness of the acid layer and outer membrane. The release rate is controlled by the inner membrane, rapid release being achieved by omitting this membrane. The dosage forms may be designed (a) so that the drug is not released significantly until the upper colon is reached, e.g. for delivery of drugs that are labile in the stomach and small intestine, drugs intended to act locally on the colon or drugs intended to act in the early morning after admin. the previous night, or (b) to provide periodic release of a drug after a single admin., thereby avoiding tolerance effects associated with continuous release.

Dwg.0/7

FILE SEGMENT: CPI GMPI

FIELD AVAILABILITY: AB; DCN

MANUAL CODES: CPI: A12-V01; B04-B04A6; B04-C02A; B04-C03B; B05-B02A3;  
B10-C02; B10-E02; B12-M10

L257 ANSWER 43 OF 43 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN

ACCESSION NUMBER: 1989-186130 [26] WPIX

DOC. NO. NON-CPI: N1989-142200

TITLE: Vehicle brake lining wear indicator - has sensor embedded in lining contacted to bridge inner and outer conductors of coaxial line.

DERWENT CLASS: Q18 Q21 Q63 X22

INVENTOR(S): FISCHER, W; KRAMER, K; SCHAUER, F

PATENT ASSIGNEE(S): (GUTE) KABELMETAL ELECTRO GMBH; (THYS) THYSSEN IND AG;  
(GUTE) KABELMETAL ELECTRO GBMH

COUNTRY COUNT: 7

## PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN	IPC
EP 321661	A	19890628	(198926)*	GE	7		
R: DE FR GB IT							
DE 3812178	A	19890629	(198927)		5		
DE 3812178	C	19900208	(199006)				
US 4890697	A	19900102	(199009)		5		
EP 321661	B	19910814	(199133)				
R: DE FR GB IT							
DE 3864249	G	19910919	(199139)				
CA 1307569	C	19920915	(199243)			F16D066-02	
SU 1769789	A3	19921015	(199343)		5	F16D066-02	

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 321661	A	EP 1988-116078	19880929
DE 3812178	A	DE 1988-3812178	19880413
US 4890697	A	US 1988-278357	19881201
CA 1307569	C	CA 1988-586157	19881216
SU 1769789	A3	SU 1988-4356727	19881109

PRIORITY APPLN. INFO: DE 1987-3743254 19871219; DE  
1988-3812178 19880413

REFERENCE PATENTS: 1.Jnl.Ref; DE 2030967; DE 2257250; EP 140241; EP 206487;  
EP 77206; FR 2450979; FR 2504226

## INT. PATENT CLASSIF.:

MAIN: F16D066-02

SECONDARY: B60T017-22; B61H007-06; G01M013-00

## BASIC ABSTRACT:

EP 321661 A UPAB: 19930923

The wear indicator uses a sensor (4) incorporated in the brake lining (1), coupled via a heat-resistant coaxial lead (5) to an evaluation device (6). The sensor is seated in a recess (3) in the brake lining and lies at a depth (L) corresp. to the min. thickness of the brake lining, so that the inner and outer conductors of the lead are bridged when the sensor is contacted.

Pref. the coaxial lead is bent in a loop within the sensor, with the outer conductor lying in the plane of the sensor end face.

1/5

FILE SEGMENT: EPI GMPI

FIELD AVAILABILITY: AB; GI

MANUAL CODES: EPI: X22-E02

=&gt; □

## TEXT SEARCH

=&gt; file hcaplus

FILE 'HCAPLUS' ENTERED AT 14:58:23 ON 07 JUL 2006

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FILE COVERS 1907 - 7 Jul 2006 VOL 145 ISS 3

FILE LAST UPDATED: 6 Jul 2006 (20060706/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

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L3	8	SEA FILE=REGISTRY ABB=ON	PLU=ON	ANGIOTENSIN CONVERTING ENZYME?/CN
L7	17	SEA FILE=REGISTRY ABB=ON	PLU=ON	ANGIOTENSIN-CONVERTING ENZYME?/CN
L8	23	SEA FILE=REGISTRY ABB=ON	PLU=ON	L7 OR L3
L10	10345	SEA FILE=HCAPLUS ABB=ON	PLU=ON	L8 (L) INHIB?/OBI
L11	9707	SEA FILE=HCAPLUS ABB=ON	PLU=ON	(ANGIOTENSIN CONVERTING ENZYME?/OBI OR ACE/OBI) (1A) INHIB?/OBI
L12	3	SEA FILE=REGISTRY ABB=ON	PLU=ON	IMIDAPRIL?/CN
L13	4	SEA FILE=REGISTRY ABB=ON	PLU=ON	FOSINOPRIL?/CN
L14	3	SEA FILE=REGISTRY ABB=ON	PLU=ON	MOEXIPRIL?/CN
L15	8	SEA FILE=REGISTRY ABB=ON	PLU=ON	PERINDOPRIL?/CN
L16	5	SEA FILE=REGISTRY ABB=ON	PLU=ON	RAMIPRIL?/CN
L17	3	SEA FILE=REGISTRY ABB=ON	PLU=ON	SPIRAPRIL?/CN
L18	6	SEA FILE=REGISTRY ABB=ON	PLU=ON	CILAZAPRIL?/CN
L19	5	SEA FILE=REGISTRY ABB=ON	PLU=ON	BENAZEPRIL?/CN
L20	4	SEA FILE=REGISTRY ABB=ON	PLU=ON	TRANDOLAPRIL?/CN
L21	41	SEA FILE=REGISTRY ABB=ON	PLU=ON	(L12 OR L13 OR L14 OR L15 OR L16 OR L17 OR L18 OR L19 OR L20)
L22	3797	SEA FILE=HCAPLUS ABB=ON	PLU=ON	L21
L23	152437	SEA FILE=HCAPLUS ABB=ON	PLU=ON	DRUG DELIVERY SYSTEMS/CT
L24	6516	SEA FILE=HCAPLUS ABB=ON	PLU=ON	L23 (L) TRANSDERM?/OBI
L29	77	SEA FILE=HCAPLUS ABB=ON	PLU=ON	(L10 OR L11 OR L22) AND L24
L30	35415	SEA FILE=HCAPLUS ABB=ON	PLU=ON	MEDICAL GOODS/CT
L31	12	SEA FILE=HCAPLUS ABB=ON	PLU=ON	L29 AND L30
L32	4111	SEA FILE=HCAPLUS ABB=ON	PLU=ON	L30 (L) (PLASTER?/OBI OR TOPICAL?/OBI OR ADHESIV?/OBI OR BANDAG?/OBI)
L33	6	SEA FILE=HCAPLUS ABB=ON	PLU=ON	L31 AND L32

=&gt; d que nos L34

L3	8	SEA FILE=REGISTRY ABB=ON	PLU=ON	ANGIOTENSIN CONVERTING ENZYME?/CN
L7	17	SEA FILE=REGISTRY ABB=ON	PLU=ON	ANGIOTENSIN-CONVERTING ENZYME?/CN
L8	23	SEA FILE=REGISTRY ABB=ON	PLU=ON	L7 OR L3
L10	10345	SEA FILE=HCAPLUS ABB=ON	PLU=ON	L8 (L) INHIB?/OBI
L11	9707	SEA FILE=HCAPLUS ABB=ON	PLU=ON	(ANGIOTENSIN CONVERTING ENZYM?/OBI OR ACE/OBI) (1A) INHIB?/OBI
L12	3	SEA FILE=REGISTRY ABB=ON	PLU=ON	IMIDAPRIL?/CN
L13	4	SEA FILE=REGISTRY ABB=ON	PLU=ON	FOSINOPRIL?/CN
L14	3	SEA FILE=REGISTRY ABB=ON	PLU=ON	MOEXIPRIL?/CN
L15	8	SEA FILE=REGISTRY ABB=ON	PLU=ON	PERINDOPRIL?/CN
L16	5	SEA FILE=REGISTRY ABB=ON	PLU=ON	RAMIPRIL?/CN
L17	3	SEA FILE=REGISTRY ABB=ON	PLU=ON	SPIRAPRIL?/CN
L18	6	SEA FILE=REGISTRY ABB=ON	PLU=ON	CILAZAPRIL?/CN
L19	5	SEA FILE=REGISTRY ABB=ON	PLU=ON	BENAZEPRIL?/CN
L20	4	SEA FILE=REGISTRY ABB=ON	PLU=ON	TRANDOLAPRIL?/CN
L21	41	SEA FILE=REGISTRY ABB=ON	PLU=ON	(L12 OR L13 OR L14 OR L15 OR L16 OR L17 OR L18 OR L19 OR L20)
L22	3797	SEA FILE=HCAPLUS ABB=ON	PLU=ON	L21
L23	152437	SEA FILE=HCAPLUS ABB=ON	PLU=ON	DRUG DELIVERY SYSTEMS/CT
L24	6516	SEA FILE=HCAPLUS ABB=ON	PLU=ON	L23 (L) TRANSDERM?/OBI
L26	1	SEA FILE=REGISTRY ABB=ON	PLU=ON	EUTANOL G/CN
L27	1	SEA FILE=REGISTRY ABB=ON	PLU=ON	SILICON DIOXIDE/CN
L29	77	SEA FILE=HCAPLUS ABB=ON	PLU=ON	(L10 OR L11 OR L22) AND L24
L34	4	SEA FILE=HCAPLUS ABB=ON	PLU=ON	L29 AND ((L26 OR L27))

=&gt; d que nos L38

L3	8	SEA FILE=REGISTRY ABB=ON	PLU=ON	ANGIOTENSIN CONVERTING ENZYME?/CN
L7	17	SEA FILE=REGISTRY ABB=ON	PLU=ON	ANGIOTENSIN-CONVERTING ENZYME?/CN
L8	23	SEA FILE=REGISTRY ABB=ON	PLU=ON	L7 OR L3
L10	10345	SEA FILE=HCAPLUS ABB=ON	PLU=ON	L8 (L) INHIB?/OBI
L11	9707	SEA FILE=HCAPLUS ABB=ON	PLU=ON	(ANGIOTENSIN CONVERTING ENZYM?/OBI OR ACE/OBI) (1A) INHIB?/OBI
L12	3	SEA FILE=REGISTRY ABB=ON	PLU=ON	IMIDAPRIL?/CN
L13	4	SEA FILE=REGISTRY ABB=ON	PLU=ON	FOSINOPRIL?/CN
L14	3	SEA FILE=REGISTRY ABB=ON	PLU=ON	MOEXIPRIL?/CN
L15	8	SEA FILE=REGISTRY ABB=ON	PLU=ON	PERINDOPRIL?/CN
L16	5	SEA FILE=REGISTRY ABB=ON	PLU=ON	RAMIPRIL?/CN
L17	3	SEA FILE=REGISTRY ABB=ON	PLU=ON	SPIRAPRIL?/CN
L18	6	SEA FILE=REGISTRY ABB=ON	PLU=ON	CILAZAPRIL?/CN
L19	5	SEA FILE=REGISTRY ABB=ON	PLU=ON	BENAZEPRIL?/CN
L20	4	SEA FILE=REGISTRY ABB=ON	PLU=ON	TRANDOLAPRIL?/CN
L21	41	SEA FILE=REGISTRY ABB=ON	PLU=ON	(L12 OR L13 OR L14 OR L15 OR L16 OR L17 OR L18 OR L19 OR L20)
L22	3797	SEA FILE=HCAPLUS ABB=ON	PLU=ON	L21
L23	152437	SEA FILE=HCAPLUS ABB=ON	PLU=ON	DRUG DELIVERY SYSTEMS/CT
L24	6516	SEA FILE=HCAPLUS ABB=ON	PLU=ON	L23 (L) TRANSDERM?/OBI
L29	77	SEA FILE=HCAPLUS ABB=ON	PLU=ON	(L10 OR L11 OR L22) AND L24
L35	1707	SEA FILE=HCAPLUS ABB=ON	PLU=ON	PERMEATION ENHANCERS/CT
L36	8	SEA FILE=HCAPLUS ABB=ON	PLU=ON	L29 AND L35
L37	225267	SEA FILE=HCAPLUS ABB=ON	PLU=ON	ADHESIV?/BI
L38	6	SEA FILE=HCAPLUS ABB=ON	PLU=ON	L36 AND L37

=&gt; d que nos L40

L3	8	SEA FILE=REGISTRY	ABB=ON	PLU=ON	ANGIOTENSIN CONVERTING ENZYME?/CN
L7	17	SEA FILE=REGISTRY	ABB=ON	PLU=ON	ANGIOTENSIN-CONVERTING ENZYME?/CN
L8	23	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L7 OR L3
L10	10345	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	L8 (L) INHIB?/OBI
L11	9707	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	(ANGIOTENSIN CONVERTING ENZYM?/OBI OR ACE/OBI) (1A) INHIB?/OBI
L12	3	SEA FILE=REGISTRY	ABB=ON	PLU=ON	IMIDAPRIL?/CN
L13	4	SEA FILE=REGISTRY	ABB=ON	PLU=ON	FOSINOPRIL?/CN
L14	3	SEA FILE=REGISTRY	ABB=ON	PLU=ON	MOEXIPRIL?/CN
L15	8	SEA FILE=REGISTRY	ABB=ON	PLU=ON	PERINDOPRIL?/CN
L16	5	SEA FILE=REGISTRY	ABB=ON	PLU=ON	RAMIPRIL?/CN
L17	3	SEA FILE=REGISTRY	ABB=ON	PLU=ON	SPIRAPRIL?/CN
L18	6	SEA FILE=REGISTRY	ABB=ON	PLU=ON	CILAZAPRIL?/CN
L19	5	SEA FILE=REGISTRY	ABB=ON	PLU=ON	BENAZEPRIL?/CN
L20	4	SEA FILE=REGISTRY	ABB=ON	PLU=ON	TRANDOLAPRIL?/CN
L21	41	SEA FILE=REGISTRY	ABB=ON	PLU=ON	(L12 OR L13 OR L14 OR L15 OR L16 OR L17 OR L18 OR L19 OR L20)
L22	3797	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	L21
L23	152437	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	DRUG DELIVERY SYSTEMS/CT
L24	6516	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	L23 (L) TRANSDERM?/OBI
L29	77	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	(L10 OR L11 OR L22) AND L24
L39	48687	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	PATCH?/BI
L40	9	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	L39 AND L29

=&gt; d que nos L44

L3	8	SEA FILE=REGISTRY	ABB=ON	PLU=ON	ANGIOTENSIN CONVERTING ENZYME?/CN
L7	17	SEA FILE=REGISTRY	ABB=ON	PLU=ON	ANGIOTENSIN-CONVERTING ENZYME?/CN
L8	23	SEA FILE=REGISTRY	ABB=ON	PLU=ON	L7 OR L3
L10	10345	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	L8 (L) INHIB?/OBI
L11	9707	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	(ANGIOTENSIN CONVERTING ENZYM?/OBI OR ACE/OBI) (1A) INHIB?/OBI
L12	3	SEA FILE=REGISTRY	ABB=ON	PLU=ON	IMIDAPRIL?/CN
L13	4	SEA FILE=REGISTRY	ABB=ON	PLU=ON	FOSINOPRIL?/CN
L14	3	SEA FILE=REGISTRY	ABB=ON	PLU=ON	MOEXIPRIL?/CN
L15	8	SEA FILE=REGISTRY	ABB=ON	PLU=ON	PERINDOPRIL?/CN
L16	5	SEA FILE=REGISTRY	ABB=ON	PLU=ON	RAMIPRIL?/CN
L17	3	SEA FILE=REGISTRY	ABB=ON	PLU=ON	SPIRAPRIL?/CN
L18	6	SEA FILE=REGISTRY	ABB=ON	PLU=ON	CILAZAPRIL?/CN
L19	5	SEA FILE=REGISTRY	ABB=ON	PLU=ON	BENAZEPRIL?/CN
L20	4	SEA FILE=REGISTRY	ABB=ON	PLU=ON	TRANDOLAPRIL?/CN
L21	41	SEA FILE=REGISTRY	ABB=ON	PLU=ON	(L12 OR L13 OR L14 OR L15 OR L16 OR L17 OR L18 OR L19 OR L20)
L22	3797	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	L21
L23	152437	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	DRUG DELIVERY SYSTEMS/CT
L24	6516	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	L23 (L) TRANSDERM?/OBI
L29	77	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	(L10 OR L11 OR L22) AND L24
L43	185223	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	MATRIX/OBI OR MATRIC?/OBI
L44	4	SEA FILE=HCAPLUS	ABB=ON	PLU=ON	L29 AND L43

=&gt; d que nos L49

L3	8	SEA FILE=REGISTRY ABB=ON	PLU=ON	ANGIOTENSIN CONVERTING ENZYME?/CN
L7	17	SEA FILE=REGISTRY ABB=ON	PLU=ON	ANGIOTENSIN-CONVERTING ENZYME?/CN
L8	23	SEA FILE=REGISTRY ABB=ON	PLU=ON	L7 OR L3
L10	10345	SEA FILE=HCAPLUS ABB=ON	PLU=ON	L8 (L) INHIB?/OBI
L11	9707	SEA FILE=HCAPLUS ABB=ON	PLU=ON	(ANGIOTENSIN CONVERTING ENZYM?/OBI OR ACE/OBI) (1A) INHIB?/OBI
L12	3	SEA FILE=REGISTRY ABB=ON	PLU=ON	IMIDAPRIL?/CN
L13	4	SEA FILE=REGISTRY ABB=ON	PLU=ON	FOSINOPRIL?/CN
L14	3	SEA FILE=REGISTRY ABB=ON	PLU=ON	MOEXIPRIL?/CN
L15	8	SEA FILE=REGISTRY ABB=ON	PLU=ON	PERINDOPRIL?/CN
L16	5	SEA FILE=REGISTRY ABB=ON	PLU=ON	RAMIPRIL?/CN
L17	3	SEA FILE=REGISTRY ABB=ON	PLU=ON	SPIRAPRIL?/CN
L18	6	SEA FILE=REGISTRY ABB=ON	PLU=ON	CILAZAPRIL?/CN
L19	5	SEA FILE=REGISTRY ABB=ON	PLU=ON	BENAZEPRIL?/CN
L20	4	SEA FILE=REGISTRY ABB=ON	PLU=ON	TRANDOLAPRIL?/CN
L21	41	SEA FILE=REGISTRY ABB=ON	PLU=ON	(L12 OR L13 OR L14 OR L15 OR L16 OR L17 OR L18 OR L19 OR L20)
L22	3797	SEA FILE=HCAPLUS ABB=ON	PLU=ON	L21
L23	152437	SEA FILE=HCAPLUS ABB=ON	PLU=ON	DRUG DELIVERY SYSTEMS/CT
L24	6516	SEA FILE=HCAPLUS ABB=ON	PLU=ON	L23 (L) TRANSDERM?/OBI
L29	77	SEA FILE=HCAPLUS ABB=ON	PLU=ON	(L10 OR L11 OR L22) AND L24
L48	14644	SEA FILE=HCAPLUS ABB=ON	PLU=ON	PLASTER?/BI
L49	2	SEA FILE=HCAPLUS ABB=ON	PLU=ON	L48 AND L29

=&gt; d que nos L68

L3	8	SEA FILE=REGISTRY ABB=ON	PLU=ON	ANGIOTENSIN CONVERTING ENZYME?/CN
L7	17	SEA FILE=REGISTRY ABB=ON	PLU=ON	ANGIOTENSIN-CONVERTING ENZYME?/CN
L8	23	SEA FILE=REGISTRY ABB=ON	PLU=ON	L7 OR L3
L10	10345	SEA FILE=HCAPLUS ABB=ON	PLU=ON	L8 (L) INHIB?/OBI
L11	9707	SEA FILE=HCAPLUS ABB=ON	PLU=ON	(ANGIOTENSIN CONVERTING ENZYM?/OBI OR ACE/OBI) (1A) INHIB?/OBI
L12	3	SEA FILE=REGISTRY ABB=ON	PLU=ON	IMIDAPRIL?/CN
L13	4	SEA FILE=REGISTRY ABB=ON	PLU=ON	FOSINOPRIL?/CN
L14	3	SEA FILE=REGISTRY ABB=ON	PLU=ON	MOEXIPRIL?/CN
L15	8	SEA FILE=REGISTRY ABB=ON	PLU=ON	PERINDOPRIL?/CN
L16	5	SEA FILE=REGISTRY ABB=ON	PLU=ON	RAMIPRIL?/CN
L17	3	SEA FILE=REGISTRY ABB=ON	PLU=ON	SPIRAPRIL?/CN
L18	6	SEA FILE=REGISTRY ABB=ON	PLU=ON	CILAZAPRIL?/CN
L19	5	SEA FILE=REGISTRY ABB=ON	PLU=ON	BENAZEPRIL?/CN
L20	4	SEA FILE=REGISTRY ABB=ON	PLU=ON	TRANDOLAPRIL?/CN
L21	41	SEA FILE=REGISTRY ABB=ON	PLU=ON	(L12 OR L13 OR L14 OR L15 OR L16 OR L17 OR L18 OR L19 OR L20)
L22	3797	SEA FILE=HCAPLUS ABB=ON	PLU=ON	L21
L59	48095	SEA FILE=HCAPLUS ABB=ON	PLU=ON	PHARMACEUTICAL DOSAGE FORMS/CT
L60	5248	SEA FILE=HCAPLUS ABB=ON	PLU=ON	L59 (L) (TRANSDERM?/OBI OR PLASTER?/OBI OR TOPICAL?/OBI OR ADHESIV?/OBI OR BANDAG?/OBI)
L61	13	SEA FILE=HCAPLUS ABB=ON	PLU=ON	(L10 OR L11 OR L22) AND L60
L64		QUE ABB=ON	PLU=ON	SALT?/CW
L65		QUE ABB=ON	PLU=ON	ESTER?/OBI
L66		QUE ABB=ON	PLU=ON	ACID?/CW
L67		QUE ABB=ON	PLU=ON	BASE?/OBI

L68                    6 SEA FILE=HCAPLUS ABB=ON   PLU=ON   L61 AND (L64 OR L65 OR L66 OR L67)

=> s (L33-L34 or L38 or L40 or L44 or L49 or L68) not L58

L258                    28 ((L33 OR L34) OR L38 OR L40 OR L44 OR L49 OR L68) NOT L58

=> file medline

FILE 'MEDLINE' ENTERED AT 14:58:29 ON 07 JUL 2006

FILE LAST UPDATED: 6 JUL 2006 (20060706/UP).   FILE COVERS 1950 TO DATE.

On December 11, 2005, the 2006 MeSH terms were loaded.

The MEDLINE reload for 2006 is now (26 Feb.) available.   For details on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>).  
See also:

<http://www.nlm.nih.gov/mesh/>  
[http://www.nlm.nih.gov/pubs/techbull/nd04/nd04\\_mesh.html](http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html)  
[http://www.nlm.nih.gov/pubs/techbull/nd05/nd05\\_med\\_data\\_changes.html](http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html)  
[http://www.nlm.nih.gov/pubs/techbull/nd05/nd05\\_2006\\_MeSH.html](http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html)

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d que nos L87

L12	3	SEA FILE=REGISTRY ABB=ON	PLU=ON	IMIDAPRIL?/CN
L13	4	SEA FILE=REGISTRY ABB=ON	PLU=ON	FOSINOPRIL?/CN
L14	3	SEA FILE=REGISTRY ABB=ON	PLU=ON	MOEXIPRIL?/CN
L15	8	SEA FILE=REGISTRY ABB=ON	PLU=ON	PERINDOPRIL?/CN
L16	5	SEA FILE=REGISTRY ABB=ON	PLU=ON	RAMIPRIL?/CN
L17	3	SEA FILE=REGISTRY ABB=ON	PLU=ON	SPIRAPRIL?/CN
L18	6	SEA FILE=REGISTRY ABB=ON	PLU=ON	CILAZAPRIL?/CN
L19	5	SEA FILE=REGISTRY ABB=ON	PLU=ON	BENAZEPRIL?/CN
L20	4	SEA FILE=REGISTRY ABB=ON	PLU=ON	TRANDOLAPRIL?/CN
L21	41	SEA FILE=REGISTRY ABB=ON	PLU=ON	(L12 OR L13 OR L14 OR L15 OR L16 OR L17 OR L18 OR L19 OR L20)
L74	30261	SEA FILE=MEDLINE ABB=ON	PLU=ON	ANGIOTENSIN-CONVERTING ENZYME INHIBITORS+NT/CT
L75	4016	SEA FILE=MEDLINE ABB=ON	PLU=ON	L21
L76	30376	SEA FILE=MEDLINE ABB=ON	PLU=ON	(L74 OR L75)
L77	8710	SEA FILE=MEDLINE ABB=ON	PLU=ON	ADMINISTRATION, CUTANEOUS/CT
L78	23	SEA FILE=MEDLINE ABB=ON	PLU=ON	L76 AND L77
L79	200468	SEA FILE=MEDLINE ABB=ON	PLU=ON	ADHESIV? OR ADHESION? OR ADHERE?
L80	43255	SEA FILE=MEDLINE ABB=ON	PLU=ON	SILICON?
L81		QUE ABB=ON	PLU=ON	ESTER? OR SALT? OR PRODRUG? OR BASE? OR ACID?
L82		QUE ABB=ON	PLU=ON	(PERMEAT? OR PENETRAT?) (W) ENHANC?
L83		QUE ABB=ON	PLU=ON	BANDAG?
L84		QUE ABB=ON	PLU=ON	PATCH?

*printed with author search*

L85 QUE ABB=ON PLU=ON MATRIX? OR MATRIC?  
L87 11 SEA FILE=MEDLINE ABB=ON PLU=ON L78 AND (L79 OR L80 OR L81 OR  
L82 OR L83 OR L84 OR L85)

=> s L87 not L254

L259

11 L87 NOT L254

*printed with author search*

=> file embase

FILE 'EMBASE' ENTERED AT 14:58:31 ON 07 JUL 2006  
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FILE COVERS 1974 TO 7 Jul 2006 (20060707/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

EMBASE is now updated daily. SDI frequency remains weekly (default)  
and biweekly.

This file contains CAS Registry Numbers for easy and accurate  
substance identification.

=> d que nos L135

L92 69828 SEA FILE=EMBASE ABB=ON PLU=ON DIPEPTIDYL CARBOXYPEPTIDASE  
INHIBITOR+NT/CT  
L105 11 SEA FILE=EMBASE ABB=ON PLU=ON L92 (L) (TP OR TD)/CT  
L134 1570 SEA FILE=EMBASE ABB=ON PLU=ON DRUG ADMINISTRATION ROUTE  
L135 1 SEA FILE=EMBASE ABB=ON PLU=ON L105 AND L134

=> d que nos L137

L92 69828 SEA FILE=EMBASE ABB=ON PLU=ON DIPEPTIDYL CARBOXYPEPTIDASE  
INHIBITOR+NT/CT  
L105 11 SEA FILE=EMBASE ABB=ON PLU=ON L92 (L) (TP OR TD)/CT  
L136 19958 SEA FILE=EMBASE ABB=ON PLU=ON ADHESIV?  
L137 1 SEA FILE=EMBASE ABB=ON PLU=ON L105 AND L136

=> d que nos L139

L92 69828 SEA FILE=EMBASE ABB=ON PLU=ON DIPEPTIDYL CARBOXYPEPTIDASE  
INHIBITOR+NT/CT  
L105 11 SEA FILE=EMBASE ABB=ON PLU=ON L92 (L) (TP OR TD)/CT  
L138 9222 SEA FILE=EMBASE ABB=ON PLU=ON DRUG PENETRATION  
L139 3 SEA FILE=EMBASE ABB=ON PLU=ON L105 AND L138

=> d que nos L133

L123 427 SEA FILE=EMBASE ABB=ON PLU=ON RAMIPRILAT  
L124 391 SEA FILE=EMBASE ABB=ON PLU=ON IMIDAPRIL##  
L125 1748 SEA FILE=EMBASE ABB=ON PLU=ON FOSIN!PRIL##  
L126 253 SEA FILE=EMBASE ABB=ON PLU=ON MOEX!PRIL##  
L127 3220 SEA FILE=EMBASE ABB=ON PLU=ON PERIND!PRIL##  
L128 5309 SEA FILE=EMBASE ABB=ON PLU=ON RAM!PRIL##  
L129 281 SEA FILE=EMBASE ABB=ON PLU=ON SPIR!PRIL##

L130 1461 SEA FILE=EMBASE ABB=ON PLU=ON CILAZ!PRIL##  
 L131 1496 SEA FILE=EMBASE ABB=ON PLU=ON BENAZ!PRIL##  
 L132 1723 SEA FILE=EMBASE ABB=ON PLU=ON TRAND!L!PRIL##  
 L133 1 SEA FILE=EMBASE ABB=ON PLU=ON (L123 OR L124 OR L125 OR L126  
 OR L127 OR L128 OR L129 OR L130 OR L131 OR L132) (L) (TP OR  
 TD)/CT

=> d que nos L146

L12 3 SEA FILE=REGISTRY ABB=ON PLU=ON IMIDAPRIL?/CN  
 L13 4 SEA FILE=REGISTRY ABB=ON PLU=ON FOSINOPRIL?/CN  
 L14 3 SEA FILE=REGISTRY ABB=ON PLU=ON MOEXIPRIL?/CN  
 L15 8 SEA FILE=REGISTRY ABB=ON PLU=ON PERINDOPRIL?/CN  
 L16 5 SEA FILE=REGISTRY ABB=ON PLU=ON RAMIPRIL?/CN  
 L17 3 SEA FILE=REGISTRY ABB=ON PLU=ON SPIRAPRIL?/CN  
 L18 6 SEA FILE=REGISTRY ABB=ON PLU=ON CILAZAPRIL?/CN  
 L19 5 SEA FILE=REGISTRY ABB=ON PLU=ON BENAZEPRIL?/CN  
 L20 4 SEA FILE=REGISTRY ABB=ON PLU=ON TRANDOLAPRIL?/CN  
 L21 41 SEA FILE=REGISTRY ABB=ON PLU=ON (L12 OR L13 OR L14 OR L15 OR  
 L16 OR L17 OR L18 OR L19 OR L20)  
 L26 1 SEA FILE=REGISTRY ABB=ON PLU=ON EUTANOL G/CN  
 L27 1 SEA FILE=REGISTRY ABB=ON PLU=ON SILICON DIOXIDE/CN  
 L92 69828 SEA FILE=EMBASE ABB=ON PLU=ON DIPEPTIDYL CARBOXYPEPTIDASE  
 INHIBITOR+NT/CT  
 L102 11458 SEA FILE=EMBASE ABB=ON PLU=ON L21  
 L103 12386 SEA FILE=EMBASE ABB=ON PLU=ON (L26 OR L27)  
 L106 11038 SEA FILE=EMBASE ABB=ON PLU=ON TRANSDERMAL DRUG ADMINISTRATION  
 /CT  
 L107 88500 SEA FILE=EMBASE ABB=ON PLU=ON TOPICAL DRUG ADMINISTRATION/CT  
 L123 427 SEA FILE=EMBASE ABB=ON PLU=ON RAMIPRILAT  
 L124 391 SEA FILE=EMBASE ABB=ON PLU=ON IMIDAPRIL##  
 L125 1748 SEA FILE=EMBASE ABB=ON PLU=ON FOSIN!PRIL##  
 L126 253 SEA FILE=EMBASE ABB=ON PLU=ON MOEX!PRIL##  
 L127 3220 SEA FILE=EMBASE ABB=ON PLU=ON PERIND!PRIL##  
 L128 5309 SEA FILE=EMBASE ABB=ON PLU=ON RAM!PRIL##  
 L129 281 SEA FILE=EMBASE ABB=ON PLU=ON SPIR!PRIL##  
 L130 1461 SEA FILE=EMBASE ABB=ON PLU=ON CILAZ!PRIL##  
 L131 1496 SEA FILE=EMBASE ABB=ON PLU=ON BENAZ!PRIL##  
 L132 1723 SEA FILE=EMBASE ABB=ON PLU=ON TRAND!L!PRIL##  
 L140 69918 SEA FILE=EMBASE ABB=ON PLU=ON L92 OR L102 OR (L123 OR L124  
 OR L125 OR L126 OR L127 OR L128 OR L129 OR L130 OR L131 OR  
 L132)  
 L144 895 SEA FILE=EMBASE ABB=ON PLU=ON L140 AND (L106 OR L107)  
 L145 305 SEA FILE=EMBASE ABB=ON PLU=ON L144 NOT ((TP OR TD)/CT)  
 L146 0 SEA FILE=EMBASE ABB=ON PLU=ON L103 AND L145

=> d que nos L164

L12 3 SEA FILE=REGISTRY ABB=ON PLU=ON IMIDAPRIL?/CN  
 L13 4 SEA FILE=REGISTRY ABB=ON PLU=ON FOSINOPRIL?/CN  
 L14 3 SEA FILE=REGISTRY ABB=ON PLU=ON MOEXIPRIL?/CN  
 L15 8 SEA FILE=REGISTRY ABB=ON PLU=ON PERINDOPRIL?/CN  
 L16 5 SEA FILE=REGISTRY ABB=ON PLU=ON RAMIPRIL?/CN  
 L17 3 SEA FILE=REGISTRY ABB=ON PLU=ON SPIRAPRIL?/CN  
 L18 6 SEA FILE=REGISTRY ABB=ON PLU=ON CILAZAPRIL?/CN  
 L19 5 SEA FILE=REGISTRY ABB=ON PLU=ON BENAZEPRIL?/CN  
 L20 4 SEA FILE=REGISTRY ABB=ON PLU=ON TRANDOLAPRIL?/CN

L21	41	SEA FILE=REGISTRY	ABB=ON	PLU=ON	(L12 OR L13 OR L14 OR L15 OR L16 OR L17 OR L18 OR L19 OR L20)
L92	69828	SEA FILE=EMBASE	ABB=ON	PLU=ON	DIPEPTIDYL CARBOXYPEPTIDASE INHIBITOR+NT/CT
L102	11458	SEA FILE=EMBASE	ABB=ON	PLU=ON	L21
L106	11038	SEA FILE=EMBASE	ABB=ON	PLU=ON	TRANSDERMAL DRUG ADMINISTRATION /CT
L107	88500	SEA FILE=EMBASE	ABB=ON	PLU=ON	TOPICAL DRUG ADMINISTRATION/CT
L123	427	SEA FILE=EMBASE	ABB=ON	PLU=ON	RAMIPRILAT
L124	391	SEA FILE=EMBASE	ABB=ON	PLU=ON	IMIDAPRIL##
L125	1748	SEA FILE=EMBASE	ABB=ON	PLU=ON	FOSIN!PRIL##
L126	253	SEA FILE=EMBASE	ABB=ON	PLU=ON	MOEX!PRIL##
L127	3220	SEA FILE=EMBASE	ABB=ON	PLU=ON	PERIND!PRIL##
L128	5309	SEA FILE=EMBASE	ABB=ON	PLU=ON	RAM!PRIL##
L129	281	SEA FILE=EMBASE	ABB=ON	PLU=ON	SPIR!PRIL##
L130	1461	SEA FILE=EMBASE	ABB=ON	PLU=ON	CILAZ!PRIL##
L131	1496	SEA FILE=EMBASE	ABB=ON	PLU=ON	BENAZ!PRIL##
L132	1723	SEA FILE=EMBASE	ABB=ON	PLU=ON	TRAND!L!PRIL##
L140	69918	SEA FILE=EMBASE	ABB=ON	PLU=ON	L92 OR L102 OR (L123 OR L124 OR L125 OR L126 OR L127 OR L128 OR L129 OR L130 OR L131 OR L132)
L144	895	SEA FILE=EMBASE	ABB=ON	PLU=ON	L140 AND (L106 OR L107)
L145	305	SEA FILE=EMBASE	ABB=ON	PLU=ON	L144 NOT ((TP OR TD)/CT)
L149		QUE	ABB=ON	PLU=ON	PATCH?
L161	18	SEA FILE=EMBASE	ABB=ON	PLU=ON	L145 AND L149
L162	11038	SEA FILE=EMBASE	ABB=ON	PLU=ON	TRANSDERMAL DRUG ADMINISTRATION /CT
L163	3870	SEA FILE=EMBASE	ABB=ON	PLU=ON	L162/MAJ
L164	1	SEA FILE=EMBASE	ABB=ON	PLU=ON	L161 AND L163

=> d que nos L165

L12	3	SEA FILE=REGISTRY	ABB=ON	PLU=ON	IMIDAPRIL?/CN
L13	4	SEA FILE=REGISTRY	ABB=ON	PLU=ON	FOSINOPRIL?/CN
L14	3	SEA FILE=REGISTRY	ABB=ON	PLU=ON	MOEXIPRIL?/CN
L15	8	SEA FILE=REGISTRY	ABB=ON	PLU=ON	PERINDOPRIL?/CN
L16	5	SEA FILE=REGISTRY	ABB=ON	PLU=ON	RAMIPRIL?/CN
L17	3	SEA FILE=REGISTRY	ABB=ON	PLU=ON	SPIRAPRIL?/CN
L18	6	SEA FILE=REGISTRY	ABB=ON	PLU=ON	CILAZAPRIL?/CN
L19	5	SEA FILE=REGISTRY	ABB=ON	PLU=ON	BENAZEPRIL?/CN
L20	4	SEA FILE=REGISTRY	ABB=ON	PLU=ON	TRANDOLAPRIL?/CN
L21	41	SEA FILE=REGISTRY	ABB=ON	PLU=ON	(L12 OR L13 OR L14 OR L15 OR L16 OR L17 OR L18 OR L19 OR L20)
L92	69828	SEA FILE=EMBASE	ABB=ON	PLU=ON	DIPEPTIDYL CARBOXYPEPTIDASE INHIBITOR+NT/CT
L102	11458	SEA FILE=EMBASE	ABB=ON	PLU=ON	L21
L106	11038	SEA FILE=EMBASE	ABB=ON	PLU=ON	TRANSDERMAL DRUG ADMINISTRATION /CT
L107	88500	SEA FILE=EMBASE	ABB=ON	PLU=ON	TOPICAL DRUG ADMINISTRATION/CT
L123	427	SEA FILE=EMBASE	ABB=ON	PLU=ON	RAMIPRILAT
L124	391	SEA FILE=EMBASE	ABB=ON	PLU=ON	IMIDAPRIL##
L125	1748	SEA FILE=EMBASE	ABB=ON	PLU=ON	FOSIN!PRIL##
L126	253	SEA FILE=EMBASE	ABB=ON	PLU=ON	MOEX!PRIL##
L127	3220	SEA FILE=EMBASE	ABB=ON	PLU=ON	PERIND!PRIL##
L128	5309	SEA FILE=EMBASE	ABB=ON	PLU=ON	RAM!PRIL##
L129	281	SEA FILE=EMBASE	ABB=ON	PLU=ON	SPIR!PRIL##
L130	1461	SEA FILE=EMBASE	ABB=ON	PLU=ON	CILAZ!PRIL##

L131 1496 SEA FILE=EMBASE ABB=ON PLU=ON BENAZ!PRIL##  
 L132 1723 SEA FILE=EMBASE ABB=ON PLU=ON TRAND!L!PRIL##  
 L140 69918 SEA FILE=EMBASE ABB=ON PLU=ON L92 OR L102 OR (L123 OR L124  
 OR L125 OR L126 OR L127 OR L128 OR L129 OR L130 OR L131 OR  
 L132)  
 L144 895 SEA FILE=EMBASE ABB=ON PLU=ON L140 AND (L106 OR L107)  
 L145 305 SEA FILE=EMBASE ABB=ON PLU=ON L144 NOT ((TP OR TD)/CT)  
 L150 QUE ABB=ON PLU=ON MATRIX? OR MATRIC?  
 L165 4 SEA FILE=EMBASE ABB=ON PLU=ON L145 AND L150

=> d que nos L166

L12 3 SEA FILE=REGISTRY ABB=ON PLU=ON IMIDAPRIL?/CN  
 L13 4 SEA FILE=REGISTRY ABB=ON PLU=ON FOSINOPRIL?/CN  
 L14 3 SEA FILE=REGISTRY ABB=ON PLU=ON MOEXIPRIL?/CN  
 L15 8 SEA FILE=REGISTRY ABB=ON PLU=ON PERINDOPRIL?/CN  
 L16 5 SEA FILE=REGISTRY ABB=ON PLU=ON RAMIPRIL?/CN  
 L17 3 SEA FILE=REGISTRY ABB=ON PLU=ON SPIRAPRIL?/CN  
 L18 6 SEA FILE=REGISTRY ABB=ON PLU=ON CILAZAPRIL?/CN  
 L19 5 SEA FILE=REGISTRY ABB=ON PLU=ON BENAZEPRIL?/CN  
 L20 4 SEA FILE=REGISTRY ABB=ON PLU=ON TRANDOLAPRIL?/CN  
 L21 41 SEA FILE=REGISTRY ABB=ON PLU=ON (L12 OR L13 OR L14 OR L15 OR  
 L16 OR L17 OR L18 OR L19 OR L20)  
 L92 69828 SEA FILE=EMBASE ABB=ON PLU=ON DIPEPTIDYL CARBOXYPEPTIDASE  
 INHIBITOR+NT/CT  
 L102 11458 SEA FILE=EMBASE ABB=ON PLU=ON L21  
 L106 11038 SEA FILE=EMBASE ABB=ON PLU=ON TRANSDERMAL DRUG ADMINISTRATION  
 /CT  
 L107 88500 SEA FILE=EMBASE ABB=ON PLU=ON TOPICAL DRUG ADMINISTRATION/CT  
  
 L123 427 SEA FILE=EMBASE ABB=ON PLU=ON RAMIPRILAT  
 L124 391 SEA FILE=EMBASE ABB=ON PLU=ON IMIDAPRIL##  
 L125 1748 SEA FILE=EMBASE ABB=ON PLU=ON FOSIN!PRIL##  
 L126 253 SEA FILE=EMBASE ABB=ON PLU=ON MOEX!PRIL##  
 L127 3220 SEA FILE=EMBASE ABB=ON PLU=ON PERIND!PRIL##  
 L128 5309 SEA FILE=EMBASE ABB=ON PLU=ON RAM!PRIL##  
 L129 281 SEA FILE=EMBASE ABB=ON PLU=ON SPIR!PRIL##  
 L130 1461 SEA FILE=EMBASE ABB=ON PLU=ON CILAZ!PRIL##  
 L131 1496 SEA FILE=EMBASE ABB=ON PLU=ON BENAZ!PRIL##  
 L132 1723 SEA FILE=EMBASE ABB=ON PLU=ON TRAND!L!PRIL##  
 L140 69918 SEA FILE=EMBASE ABB=ON PLU=ON L92 OR L102 OR (L123 OR L124  
 OR L125 OR L126 OR L127 OR L128 OR L129 OR L130 OR L131 OR  
 L132)  
 L144 895 SEA FILE=EMBASE ABB=ON PLU=ON L140 AND (L106 OR L107)  
 L145 305 SEA FILE=EMBASE ABB=ON PLU=ON L144 NOT ((TP OR TD)/CT)  
 L151 QUE ABB=ON PLU=ON BANDAG?  
 L166 0 SEA FILE=EMBASE ABB=ON PLU=ON L145 AND L151

=> d que nos L168

L12 3 SEA FILE=REGISTRY ABB=ON PLU=ON IMIDAPRIL?/CN  
 L13 4 SEA FILE=REGISTRY ABB=ON PLU=ON FOSINOPRIL?/CN  
 L14 3 SEA FILE=REGISTRY ABB=ON PLU=ON MOEXIPRIL?/CN  
 L15 8 SEA FILE=REGISTRY ABB=ON PLU=ON PERINDOPRIL?/CN  
 L16 5 SEA FILE=REGISTRY ABB=ON PLU=ON RAMIPRIL?/CN  
 L17 3 SEA FILE=REGISTRY ABB=ON PLU=ON SPIRAPRIL?/CN  
 L18 6 SEA FILE=REGISTRY ABB=ON PLU=ON CILAZAPRIL?/CN  
 L19 5 SEA FILE=REGISTRY ABB=ON PLU=ON BENAZEPRIL?/CN

L20 4 SEA FILE=REGISTRY ABB=ON PLU=ON TRANDOLAPRIL?/CN  
 L21 41 SEA FILE=REGISTRY ABB=ON PLU=ON (L12 OR L13 OR L14 OR L15 OR  
 L16 OR L17 OR L18 OR L19 OR L20)  
 L92 69828 SEA FILE=EMBASE ABB=ON PLU=ON DIPEPTIDYL CARBOXYPEPTIDASE  
 INHIBITOR+NT/CT  
 L102 11458 SEA FILE=EMBASE ABB=ON PLU=ON L21  
 L106 11038 SEA FILE=EMBASE ABB=ON PLU=ON TRANSDERMAL DRUG ADMINISTRATION  
 /CT  
 L107 88500 SEA FILE=EMBASE ABB=ON PLU=ON TOPICAL DRUG ADMINISTRATION/CT  
  
 L123 427 SEA FILE=EMBASE ABB=ON PLU=ON RAMIPRILAT  
 L124 391 SEA FILE=EMBASE ABB=ON PLU=ON IMIDAPRIL##  
 L125 1748 SEA FILE=EMBASE ABB=ON PLU=ON FOSIN!PRIL##  
 L126 253 SEA FILE=EMBASE ABB=ON PLU=ON MOEX!PRIL##  
 L127 3220 SEA FILE=EMBASE ABB=ON PLU=ON PERIND!PRIL##  
 L128 5309 SEA FILE=EMBASE ABB=ON PLU=ON RAM!PRIL##  
 L129 281 SEA FILE=EMBASE ABB=ON PLU=ON SPIR!PRIL##  
 L130 1461 SEA FILE=EMBASE ABB=ON PLU=ON CILAZ!PRIL##  
 L131 1496 SEA FILE=EMBASE ABB=ON PLU=ON BENAZ!PRIL##  
 L132 1723 SEA FILE=EMBASE ABB=ON PLU=ON TRAND!L!PRIL##  
 L140 69918 SEA FILE=EMBASE ABB=ON PLU=ON L92 OR L102 OR (L123 OR L124  
 OR L125 OR L126 OR L127 OR L128 OR L129 OR L130 OR L131 OR  
 L132)  
 L144 895 SEA FILE=EMBASE ABB=ON PLU=ON L140 AND (L106 OR L107)  
 L152 QUE ABB=ON PLU=ON (PERMEAT? OR PENETRAT?) (1A) ENHANC?  
 L168 2 SEA FILE=EMBASE ABB=ON PLU=ON L144 AND L152

=> d que nos L171

L12 3 SEA FILE=REGISTRY ABB=ON PLU=ON IMIDAPRIL?/CN  
 L13 4 SEA FILE=REGISTRY ABB=ON PLU=ON FOSINOPRIL?/CN  
 L14 3 SEA FILE=REGISTRY ABB=ON PLU=ON MOEXIPRIL?/CN  
 L15 8 SEA FILE=REGISTRY ABB=ON PLU=ON PERINDOPRIL?/CN  
 L16 5 SEA FILE=REGISTRY ABB=ON PLU=ON RAMIPRIL?/CN  
 L17 3 SEA FILE=REGISTRY ABB=ON PLU=ON SPIRAPRIL?/CN  
 L18 6 SEA FILE=REGISTRY ABB=ON PLU=ON CILAZAPRIL?/CN  
 L19 5 SEA FILE=REGISTRY ABB=ON PLU=ON BENAZEPRIL?/CN  
 L20 4 SEA FILE=REGISTRY ABB=ON PLU=ON TRANDOLAPRIL?/CN  
 L21 41 SEA FILE=REGISTRY ABB=ON PLU=ON (L12 OR L13 OR L14 OR L15 OR  
 L16 OR L17 OR L18 OR L19 OR L20)  
 L92 69828 SEA FILE=EMBASE ABB=ON PLU=ON DIPEPTIDYL CARBOXYPEPTIDASE  
 INHIBITOR+NT/CT  
 L102 11458 SEA FILE=EMBASE ABB=ON PLU=ON L21  
 L106 11038 SEA FILE=EMBASE ABB=ON PLU=ON TRANSDERMAL DRUG ADMINISTRATION  
 /CT  
 L107 88500 SEA FILE=EMBASE ABB=ON PLU=ON TOPICAL DRUG ADMINISTRATION/CT  
  
 L123 427 SEA FILE=EMBASE ABB=ON PLU=ON RAMIPRILAT  
 L124 391 SEA FILE=EMBASE ABB=ON PLU=ON IMIDAPRIL##  
 L125 1748 SEA FILE=EMBASE ABB=ON PLU=ON FOSIN!PRIL##  
 L126 253 SEA FILE=EMBASE ABB=ON PLU=ON MOEX!PRIL##  
 L127 3220 SEA FILE=EMBASE ABB=ON PLU=ON PERIND!PRIL##  
 L128 5309 SEA FILE=EMBASE ABB=ON PLU=ON RAM!PRIL##  
 L129 281 SEA FILE=EMBASE ABB=ON PLU=ON SPIR!PRIL##  
 L130 1461 SEA FILE=EMBASE ABB=ON PLU=ON CILAZ!PRIL##  
 L131 1496 SEA FILE=EMBASE ABB=ON PLU=ON BENAZ!PRIL##  
 L132 1723 SEA FILE=EMBASE ABB=ON PLU=ON TRAND!L!PRIL##  
 L140 69918 SEA FILE=EMBASE ABB=ON PLU=ON L92 OR L102 OR (L123 OR L124  
 OR L125 OR L126 OR L127 OR L128 OR L129 OR L130 OR L131 OR

L132)  
 L144 895 SEA FILE=EMBASE ABB=ON PLU=ON L140 AND (L106 OR L107)  
 L145 305 SEA FILE=EMBASE ABB=ON PLU=ON L144 NOT ((TP OR TD)/CT)  
 L153 QUE ABB=ON PLU=ON PRODRUG?  
 L169 6 SEA FILE=EMBASE ABB=ON PLU=ON L145 AND L153  
 L170 2894 SEA FILE=EMBASE ABB=ON PLU=ON SKIN PERMEABILITY  
 L171 1 SEA FILE=EMBASE ABB=ON PLU=ON L169 AND L170

=> d que nos L173

L12 3 SEA FILE=REGISTRY ABB=ON PLU=ON IMIDAPRIL?/CN  
 L13 4 SEA FILE=REGISTRY ABB=ON PLU=ON FOSINOPRIL?/CN  
 L14 3 SEA FILE=REGISTRY ABB=ON PLU=ON MOEXIPRIL?/CN  
 L15 8 SEA FILE=REGISTRY ABB=ON PLU=ON PERINDOPRIL?/CN  
 L16 5 SEA FILE=REGISTRY ABB=ON PLU=ON RAMIPRIL?/CN  
 L17 3 SEA FILE=REGISTRY ABB=ON PLU=ON SPIRAPRIL?/CN  
 L18 6 SEA FILE=REGISTRY ABB=ON PLU=ON CILAZAPRIL?/CN  
 L19 5 SEA FILE=REGISTRY ABB=ON PLU=ON BENAZEPRIL?/CN  
 L20 4 SEA FILE=REGISTRY ABB=ON PLU=ON TRANDOLAPRIL?/CN  
 L21 41 SEA FILE=REGISTRY ABB=ON PLU=ON (L12 OR L13 OR L14 OR L15 OR  
 L16 OR L17 OR L18 OR L19 OR L20)  
 L92 69828 SEA FILE=EMBASE ABB=ON PLU=ON DIPEPTIDYL CARBOXYPEPTIDASE  
 INHIBITOR+NT/CT  
 L102 11458 SEA FILE=EMBASE ABB=ON PLU=ON L21  
 L106 11038 SEA FILE=EMBASE ABB=ON PLU=ON TRANSDERMAL DRUG ADMINISTRATION  
 /CT  
 L107 88500 SEA FILE=EMBASE ABB=ON PLU=ON TOPICAL DRUG ADMINISTRATION/CT  
 L123 427 SEA FILE=EMBASE ABB=ON PLU=ON RAMIPRILAT  
 L124 391 SEA FILE=EMBASE ABB=ON PLU=ON IMIDAPRIL##  
 L125 1748 SEA FILE=EMBASE ABB=ON PLU=ON FOSIN!PRIL##  
 L126 253 SEA FILE=EMBASE ABB=ON PLU=ON MOEX!PRIL##  
 L127 3220 SEA FILE=EMBASE ABB=ON PLU=ON PERIND!PRIL##  
 L128 5309 SEA FILE=EMBASE ABB=ON PLU=ON RAM!PRIL##  
 L129 281 SEA FILE=EMBASE ABB=ON PLU=ON SPIR!PRIL##  
 L130 1461 SEA FILE=EMBASE ABB=ON PLU=ON CILAZ!PRIL##  
 L131 1496 SEA FILE=EMBASE ABB=ON PLU=ON BENAZ!PRIL##  
 L132 1723 SEA FILE=EMBASE ABB=ON PLU=ON TRAND!L!PRIL##  
 L140 69918 SEA FILE=EMBASE ABB=ON PLU=ON L92 OR L102 OR (L123 OR L124  
 OR L125 OR L126 OR L127 OR L128 OR L129 OR L130 OR L131 OR  
 L132)  
 L144 895 SEA FILE=EMBASE ABB=ON PLU=ON L140 AND (L106 OR L107)  
 L154 QUE ABB=ON PLU=ON ADHESIV?  
 L173 2 SEA FILE=EMBASE ABB=ON PLU=ON L144 AND L154

=> d que nos L175

L12 3 SEA FILE=REGISTRY ABB=ON PLU=ON IMIDAPRIL?/CN  
 L13 4 SEA FILE=REGISTRY ABB=ON PLU=ON FOSINOPRIL?/CN  
 L14 3 SEA FILE=REGISTRY ABB=ON PLU=ON MOEXIPRIL?/CN  
 L15 8 SEA FILE=REGISTRY ABB=ON PLU=ON PERINDOPRIL?/CN  
 L16 5 SEA FILE=REGISTRY ABB=ON PLU=ON RAMIPRIL?/CN  
 L17 3 SEA FILE=REGISTRY ABB=ON PLU=ON SPIRAPRIL?/CN  
 L18 6 SEA FILE=REGISTRY ABB=ON PLU=ON CILAZAPRIL?/CN  
 L19 5 SEA FILE=REGISTRY ABB=ON PLU=ON BENAZEPRIL?/CN  
 L20 4 SEA FILE=REGISTRY ABB=ON PLU=ON TRANDOLAPRIL?/CN  
 L21 41 SEA FILE=REGISTRY ABB=ON PLU=ON (L12 OR L13 OR L14 OR L15 OR  
 L16 OR L17 OR L18 OR L19 OR L20)

L92	69828	SEA FILE=EMBASE ABB=ON	PLU=ON	DIPEPTIDYL CARBOXYPEPTIDASE INHIBITOR+NT/CT
L102	11458	SEA FILE=EMBASE ABB=ON	PLU=ON	L21
L106	11038	SEA FILE=EMBASE ABB=ON	PLU=ON	TRANSDERMAL DRUG ADMINISTRATION /CT
L107	88500	SEA FILE=EMBASE ABB=ON	PLU=ON	TOPICAL DRUG ADMINISTRATION/CT
L123	427	SEA FILE=EMBASE ABB=ON	PLU=ON	RAMIPRILAT
L124	391	SEA FILE=EMBASE ABB=ON	PLU=ON	IMIDAPRIL##
L125	1748	SEA FILE=EMBASE ABB=ON	PLU=ON	FOSIN!PRIL##
L126	253	SEA FILE=EMBASE ABB=ON	PLU=ON	MOEX!PRIL##
L127	3220	SEA FILE=EMBASE ABB=ON	PLU=ON	PERIND!PRIL##
L128	5309	SEA FILE=EMBASE ABB=ON	PLU=ON	RAM!PRIL##
L129	281	SEA FILE=EMBASE ABB=ON	PLU=ON	SPIR!PRIL##
L130	1461	SEA FILE=EMBASE ABB=ON	PLU=ON	CILAZ!PRIL##
L131	1496	SEA FILE=EMBASE ABB=ON	PLU=ON	BENAZ!PRIL##
L132	1723	SEA FILE=EMBASE ABB=ON	PLU=ON	TRAND!L!PRIL##
L140	69918	SEA FILE=EMBASE ABB=ON	PLU=ON	L92 OR L102 OR (L123 OR L124 OR L125 OR L126 OR L127 OR L128 OR L129 OR L130 OR L131 OR L132)
L144	895	SEA FILE=EMBASE ABB=ON	PLU=ON	L140 AND (L106 OR L107)
L155		QUE ABB=ON PLU=ON PLASTER?		
L175	0	SEA FILE=EMBASE ABB=ON	PLU=ON	L144 AND L155

=> d que nos L177

L12	3	SEA FILE=REGISTRY ABB=ON	PLU=ON	IMIDAPRIL?/CN
L13	4	SEA FILE=REGISTRY ABB=ON	PLU=ON	FOSINOPRIL?/CN
L14	3	SEA FILE=REGISTRY ABB=ON	PLU=ON	MOEXIPRIL?/CN
L15	8	SEA FILE=REGISTRY ABB=ON	PLU=ON	PERINDOPRIL?/CN
L16	5	SEA FILE=REGISTRY ABB=ON	PLU=ON	RAMIPRIL?/CN
L17	3	SEA FILE=REGISTRY ABB=ON	PLU=ON	SPIRAPRIL?/CN
L18	6	SEA FILE=REGISTRY ABB=ON	PLU=ON	CILAZAPRIL?/CN
L19	5	SEA FILE=REGISTRY ABB=ON	PLU=ON	BENAZEPRIL?/CN
L20	4	SEA FILE=REGISTRY ABB=ON	PLU=ON	TRANDOLAPRIL?/CN
L21	41	SEA FILE=REGISTRY ABB=ON	PLU=ON	(L12 OR L13 OR L14 OR L15 OR L16 OR L17 OR L18 OR L19 OR L20)
L92	69828	SEA FILE=EMBASE ABB=ON	PLU=ON	DIPEPTIDYL CARBOXYPEPTIDASE INHIBITOR+NT/CT
L102	11458	SEA FILE=EMBASE ABB=ON	PLU=ON	L21
L106	11038	SEA FILE=EMBASE ABB=ON	PLU=ON	TRANSDERMAL DRUG ADMINISTRATION /CT
L107	88500	SEA FILE=EMBASE ABB=ON	PLU=ON	TOPICAL DRUG ADMINISTRATION/CT
L123	427	SEA FILE=EMBASE ABB=ON	PLU=ON	RAMIPRILAT
L124	391	SEA FILE=EMBASE ABB=ON	PLU=ON	IMIDAPRIL##
L125	1748	SEA FILE=EMBASE ABB=ON	PLU=ON	FOSIN!PRIL##
L126	253	SEA FILE=EMBASE ABB=ON	PLU=ON	MOEX!PRIL##
L127	3220	SEA FILE=EMBASE ABB=ON	PLU=ON	PERIND!PRIL##
L128	5309	SEA FILE=EMBASE ABB=ON	PLU=ON	RAM!PRIL##
L129	281	SEA FILE=EMBASE ABB=ON	PLU=ON	SPIR!PRIL##
L130	1461	SEA FILE=EMBASE ABB=ON	PLU=ON	CILAZ!PRIL##
L131	1496	SEA FILE=EMBASE ABB=ON	PLU=ON	BENAZ!PRIL##
L132	1723	SEA FILE=EMBASE ABB=ON	PLU=ON	TRAND!L!PRIL##
L140	69918	SEA FILE=EMBASE ABB=ON	PLU=ON	L92 OR L102 OR (L123 OR L124 OR L125 OR L126 OR L127 OR L128 OR L129 OR L130 OR L131 OR L132)
L144	895	SEA FILE=EMBASE ABB=ON	PLU=ON	L140 AND (L106 OR L107)
L145	305	SEA FILE=EMBASE ABB=ON	PLU=ON	L144 NOT ((TP OR TD)/CT)

L158           QUE ABB=ON PLU=ON BASE OR BASES  
L176           2 SEA FILE=EMBASE ABB=ON PLU=ON L145 AND L158  
L177           1 SEA FILE=EMBASE ABB=ON PLU=ON GEL AND L176

=> d que nos L179

L12           3 SEA FILE=REGISTRY ABB=ON PLU=ON IMIDAPRIL?/CN  
L13           4 SEA FILE=REGISTRY ABB=ON PLU=ON FOSINOPRIL?/CN  
L14           3 SEA FILE=REGISTRY ABB=ON PLU=ON MOEXIPRIL?/CN  
L15           8 SEA FILE=REGISTRY ABB=ON PLU=ON PERINDOPRIL?/CN  
L16           5 SEA FILE=REGISTRY ABB=ON PLU=ON RAMIPRIL?/CN  
L17           3 SEA FILE=REGISTRY ABB=ON PLU=ON SPIRAPRIL?/CN  
L18           6 SEA FILE=REGISTRY ABB=ON PLU=ON CILAZAPRIL?/CN  
L19           5 SEA FILE=REGISTRY ABB=ON PLU=ON BENAZEPRIL?/CN  
L20           4 SEA FILE=REGISTRY ABB=ON PLU=ON TRANDOLAPRIL?/CN  
L21           41 SEA FILE=REGISTRY ABB=ON PLU=ON (L12 OR L13 OR L14 OR L15 OR  
              L16 OR L17 OR L18 OR L19 OR L20)  
L92           69828 SEA FILE=EMBASE ABB=ON PLU=ON DIPEPTIDYL CARBOXYPEPTIDASE  
              INHIBITOR+NT/CT  
L102           11458 SEA FILE=EMBASE ABB=ON PLU=ON L21  
L106           11038 SEA FILE=EMBASE ABB=ON PLU=ON TRANSDERMAL DRUG ADMINISTRATION  
              /CT  
L107           88500 SEA FILE=EMBASE ABB=ON PLU=ON TOPICAL DRUG ADMINISTRATION/CT  
  
L123           427 SEA FILE=EMBASE ABB=ON PLU=ON RAMIPRILAT  
L124           391 SEA FILE=EMBASE ABB=ON PLU=ON IMIDAPRIL##  
L125           1748 SEA FILE=EMBASE ABB=ON PLU=ON FOSIN!PRIL##  
L126           253 SEA FILE=EMBASE ABB=ON PLU=ON MOEX!PRIL##  
L127           3220 SEA FILE=EMBASE ABB=ON PLU=ON PERIND!PRIL##  
L128           5309 SEA FILE=EMBASE ABB=ON PLU=ON RAM!PRIL##  
L129           281 SEA FILE=EMBASE ABB=ON PLU=ON SPIR!PRIL##  
L130           1461 SEA FILE=EMBASE ABB=ON PLU=ON CILAZ!PRIL##  
L131           1496 SEA FILE=EMBASE ABB=ON PLU=ON BENAZ!PRIL##  
L132           1723 SEA FILE=EMBASE ABB=ON PLU=ON TRAND!L!PRIL##  
L140           69918 SEA FILE=EMBASE ABB=ON PLU=ON L92 OR L102 OR (L123 OR L124  
              OR L125 OR L126 OR L127 OR L128 OR L129 OR L130 OR L131 OR  
              L132)  
L144           895 SEA FILE=EMBASE ABB=ON PLU=ON L140 AND (L106 OR L107)  
L145           305 SEA FILE=EMBASE ABB=ON PLU=ON L144 NOT ((TP OR TD)/CT)  
L156           QUE ABB=ON PLU=ON ESTER?  
L170           2894 SEA FILE=EMBASE ABB=ON PLU=ON SKIN PERMEABILITY  
L178           7 SEA FILE=EMBASE ABB=ON PLU=ON L156 AND L145  
L179           2 SEA FILE=EMBASE ABB=ON PLU=ON L178 AND L170

=> s (L135 or L137 or L139 or L133 or L146 or L164 or L165 or L166 or L168 or L171  
or L173 or L175 or L177 or L179) not L255

L260           15 (L135 OR L137 OR L139 OR L133 OR L146 OR L164 OR L165 OR L166  
              OR L168 OR L171 OR L173 OR L175 OR L177 OR L179) NOT L255

=> file biosis

FILE 'BIOSIS' ENTERED AT 14:58:43 ON 07 JUL 2006  
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FILE COVERS 1969 TO DATE.  
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT  
FROM JANUARY 1969 TO DATE.

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author  
search*

RECORDS LAST ADDED: 5 July 2006 (20060705/ED)

=> d que nos L190

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L183      9251 SEA FILE=BIOSIS ABB=ON  PLU=ON  ACE INHIBITOR?
L184      7150 SEA FILE=BIOSIS ABB=ON  PLU=ON  TRANSDERMAL
L186       14 SEA FILE=BIOSIS ABB=ON  PLU=ON  L184 AND L183
L187     1573 SEA FILE=BIOSIS ABB=ON  PLU=ON  TRANSDERM? (W) ADMINISTR?
L188       5 SEA FILE=BIOSIS ABB=ON  PLU=ON  L186 AND L187
L189     148 SEA FILE=BIOSIS ABB=ON  PLU=ON  (TRANSDERM? (W) ADMINISTR?
          )/TI
L190       2 SEA FILE=BIOSIS ABB=ON  PLU=ON  L189 AND L188
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=> s L190 not L208

L261 1 L190 NOT (L208)

*printed with author search*

=> file drugu

FILE 'DRUGU' ENTERED AT 14:58:45 ON 07 JUL 2006  
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FILE LAST UPDATED: 3 JUL 2006 <20060703/UP>  
>>> DERWENT DRUG FILE (SUBSCRIBER) <<<

>>> FILE COVERS 1983 TO DATE <<<  
>>> THESAURUS AVAILABLE IN /CT <<<

=> d que nos L215

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L124      391 SEA FILE=EMBASE ABB=ON  PLU=ON  IMIDAPRIL##
L125     1748 SEA FILE=EMBASE ABB=ON  PLU=ON  FOSIN!PRIL##
L126      253 SEA FILE=EMBASE ABB=ON  PLU=ON  MOEX!PRIL##
L127     3220 SEA FILE=EMBASE ABB=ON  PLU=ON  PERIND!PRIL##
L128     5309 SEA FILE=EMBASE ABB=ON  PLU=ON  RAM!PRIL##
L129      281 SEA FILE=EMBASE ABB=ON  PLU=ON  SPIR!PRIL##
L130     1461 SEA FILE=EMBASE ABB=ON  PLU=ON  CILAZ!PRIL##
L131     1496 SEA FILE=EMBASE ABB=ON  PLU=ON  BENAZ!PRIL##
L132     1723 SEA FILE=EMBASE ABB=ON  PLU=ON  TRAND!L!PRIL##
L209     6308 SEA FILE=DRUGU ABB=ON  PLU=ON  (L124 OR L125 OR L126 OR L127
          OR L128 OR L129 OR L130 OR L131 OR L132)
L210     19007 SEA FILE=DRUGU ABB=ON  PLU=ON  ACE INHIBITOR?
L211     2457 SEA FILE=DRUGU ABB=ON  PLU=ON  ANGIOTENSIN CONVERTING ENZYME
          INHIBITOR
L212     8522 SEA FILE=DRUGU ABB=ON  PLU=ON  PATCH?
L213      90 SEA FILE=DRUGU ABB=ON  PLU=ON  (L209 OR L210 OR L211) AND L212

L214     14371 SEA FILE=DRUGU ABB=ON  PLU=ON  MATRIX? OR MATRIC?
L215      1 SEA FILE=DRUGU ABB=ON  PLU=ON  L214 AND L213
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=> d que nos L217

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L124      391 SEA FILE=EMBASE ABB=ON  PLU=ON  IMIDAPRIL##
L125     1748 SEA FILE=EMBASE ABB=ON  PLU=ON  FOSIN!PRIL##
L126      253 SEA FILE=EMBASE ABB=ON  PLU=ON  MOEX!PRIL##
```

```

L127      3220 SEA FILE=EMBASE ABB=ON  PLU=ON  PERIND!PRIL##
L128      5309 SEA FILE=EMBASE ABB=ON  PLU=ON  RAM!PRIL##
L129      281  SEA FILE=EMBASE ABB=ON  PLU=ON  SPIR!PRIL##
L130      1461 SEA FILE=EMBASE ABB=ON  PLU=ON  CILAZ!PRIL##
L131      1496 SEA FILE=EMBASE ABB=ON  PLU=ON  BENAZ!PRIL##
L132      1723 SEA FILE=EMBASE ABB=ON  PLU=ON  TRAND!L!PRIL##
L209      6308 SEA FILE=DRUGU ABB=ON  PLU=ON  (L124 OR L125 OR L126 OR L127
OR L128 OR L129 OR L130 OR L131 OR L132)
L210      19007 SEA FILE=DRUGU ABB=ON  PLU=ON  ACE INHIBITOR?
L211      2457 SEA FILE=DRUGU ABB=ON  PLU=ON  ANGIOTENSIN CONVERTING ENZYME
INHIBITOR
L212      8522 SEA FILE=DRUGU ABB=ON  PLU=ON  PATCH?
L213      90  SEA FILE=DRUGU ABB=ON  PLU=ON  (L209 OR L210 OR L211) AND L212

L216      2850 SEA FILE=DRUGU ABB=ON  PLU=ON  SILICON?
L217      0   SEA FILE=DRUGU ABB=ON  PLU=ON  L216 AND L213

```

=> d que nos L219

```

L124      391  SEA FILE=EMBASE ABB=ON  PLU=ON  IMIDAPRIL##
L125      1748 SEA FILE=EMBASE ABB=ON  PLU=ON  FOSIN!PRIL##
L126      253  SEA FILE=EMBASE ABB=ON  PLU=ON  MOEX!PRIL##
L127      3220 SEA FILE=EMBASE ABB=ON  PLU=ON  PERIND!PRIL##
L128      5309 SEA FILE=EMBASE ABB=ON  PLU=ON  RAM!PRIL##
L129      281  SEA FILE=EMBASE ABB=ON  PLU=ON  SPIR!PRIL##
L130      1461 SEA FILE=EMBASE ABB=ON  PLU=ON  CILAZ!PRIL##
L131      1496 SEA FILE=EMBASE ABB=ON  PLU=ON  BENAZ!PRIL##
L132      1723 SEA FILE=EMBASE ABB=ON  PLU=ON  TRAND!L!PRIL##
L209      6308 SEA FILE=DRUGU ABB=ON  PLU=ON  (L124 OR L125 OR L126 OR L127
OR L128 OR L129 OR L130 OR L131 OR L132)
L210      19007 SEA FILE=DRUGU ABB=ON  PLU=ON  ACE INHIBITOR?
L211      2457 SEA FILE=DRUGU ABB=ON  PLU=ON  ANGIOTENSIN CONVERTING ENZYME
INHIBITOR
L212      8522 SEA FILE=DRUGU ABB=ON  PLU=ON  PATCH?
L213      90  SEA FILE=DRUGU ABB=ON  PLU=ON  (L209 OR L210 OR L211) AND L212

L218      6737 SEA FILE=DRUGU ABB=ON  PLU=ON  (PERMEAT? OR PENETRAT?) (1A)
ENHANC?
L219      1   SEA FILE=DRUGU ABB=ON  PLU=ON  L218 AND L213

```

=> d que nos L221

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L124      391  SEA FILE=EMBASE ABB=ON  PLU=ON  IMIDAPRIL##
L125      1748 SEA FILE=EMBASE ABB=ON  PLU=ON  FOSIN!PRIL##
L126      253  SEA FILE=EMBASE ABB=ON  PLU=ON  MOEX!PRIL##
L127      3220 SEA FILE=EMBASE ABB=ON  PLU=ON  PERIND!PRIL##
L128      5309 SEA FILE=EMBASE ABB=ON  PLU=ON  RAM!PRIL##
L129      281  SEA FILE=EMBASE ABB=ON  PLU=ON  SPIR!PRIL##
L130      1461 SEA FILE=EMBASE ABB=ON  PLU=ON  CILAZ!PRIL##
L131      1496 SEA FILE=EMBASE ABB=ON  PLU=ON  BENAZ!PRIL##
L132      1723 SEA FILE=EMBASE ABB=ON  PLU=ON  TRAND!L!PRIL##
L209      6308 SEA FILE=DRUGU ABB=ON  PLU=ON  (L124 OR L125 OR L126 OR L127
OR L128 OR L129 OR L130 OR L131 OR L132)
L210      19007 SEA FILE=DRUGU ABB=ON  PLU=ON  ACE INHIBITOR?
L211      2457 SEA FILE=DRUGU ABB=ON  PLU=ON  ANGIOTENSIN CONVERTING ENZYME
INHIBITOR
L212      8522 SEA FILE=DRUGU ABB=ON  PLU=ON  PATCH?
L213      90  SEA FILE=DRUGU ABB=ON  PLU=ON  (L209 OR L210 OR L211) AND L212

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L220 1886 SEA FILE=DRUGU ABB=ON PLU=ON ADHESIV?  
L221 1 SEA FILE=DRUGU ABB=ON PLU=ON L220 AND L213

=> d que nos L222

L124 391 SEA FILE=EMBASE ABB=ON PLU=ON IMIDAPRIL##  
L125 1748 SEA FILE=EMBASE ABB=ON PLU=ON FOSIN!PRIL##  
L126 253 SEA FILE=EMBASE ABB=ON PLU=ON MOEX!PRIL##  
L127 3220 SEA FILE=EMBASE ABB=ON PLU=ON PERIND!PRIL##  
L128 5309 SEA FILE=EMBASE ABB=ON PLU=ON RAM!PRIL##  
L129 281 SEA FILE=EMBASE ABB=ON PLU=ON SPIR!PRIL##  
L130 1461 SEA FILE=EMBASE ABB=ON PLU=ON CILAZ!PRIL##  
L131 1496 SEA FILE=EMBASE ABB=ON PLU=ON BENAZ!PRIL##  
L132 1723 SEA FILE=EMBASE ABB=ON PLU=ON TRAND!L!PRIL##  
L209 6308 SEA FILE=DRUGU ABB=ON PLU=ON (L124 OR L125 OR L126 OR L127  
OR L128 OR L129 OR L130 OR L131 OR L132)  
L210 19007 SEA FILE=DRUGU ABB=ON PLU=ON ACE INHIBITOR?  
L211 2457 SEA FILE=DRUGU ABB=ON PLU=ON ANGIOTENSIN CONVERTING ENZYME  
INHIBITOR  
L212 8522 SEA FILE=DRUGU ABB=ON PLU=ON PATCH?  
L213 90 SEA FILE=DRUGU ABB=ON PLU=ON (L209 OR L210 OR L211) AND L212  
L222 0 SEA FILE=DRUGU ABB=ON PLU=ON BANDAG? AND L213

=> d que nos L223

L124 391 SEA FILE=EMBASE ABB=ON PLU=ON IMIDAPRIL##  
L125 1748 SEA FILE=EMBASE ABB=ON PLU=ON FOSIN!PRIL##  
L126 253 SEA FILE=EMBASE ABB=ON PLU=ON MOEX!PRIL##  
L127 3220 SEA FILE=EMBASE ABB=ON PLU=ON PERIND!PRIL##  
L128 5309 SEA FILE=EMBASE ABB=ON PLU=ON RAM!PRIL##  
L129 281 SEA FILE=EMBASE ABB=ON PLU=ON SPIR!PRIL##  
L130 1461 SEA FILE=EMBASE ABB=ON PLU=ON CILAZ!PRIL##  
L131 1496 SEA FILE=EMBASE ABB=ON PLU=ON BENAZ!PRIL##  
L132 1723 SEA FILE=EMBASE ABB=ON PLU=ON TRAND!L!PRIL##  
L209 6308 SEA FILE=DRUGU ABB=ON PLU=ON (L124 OR L125 OR L126 OR L127  
OR L128 OR L129 OR L130 OR L131 OR L132)  
L210 19007 SEA FILE=DRUGU ABB=ON PLU=ON ACE INHIBITOR?  
L211 2457 SEA FILE=DRUGU ABB=ON PLU=ON ANGIOTENSIN CONVERTING ENZYME  
INHIBITOR  
L212 8522 SEA FILE=DRUGU ABB=ON PLU=ON PATCH?  
L213 90 SEA FILE=DRUGU ABB=ON PLU=ON (L209 OR L210 OR L211) AND L212  
L223 2 SEA FILE=DRUGU ABB=ON PLU=ON PLASTER? AND L213

=> s (L215 or L217 or L219 or L221-L223) not L238

L262 3 (L215 OR L217 OR L219 OR (L221 OR L222 OR L223)) NOT L238

=> file wpix

FILE 'WPIX' ENTERED AT 14:58:53 ON 07 JUL 2006  
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FILE LAST UPDATED: 6 JUL 2006 <20060706/UP>  
MOST RECENT DERWENT UPDATE: 200643 <200643/DW>

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author  
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<http://scientific.thomson.com/media/scpdf/ipcrdpi.pdf> <<<

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[http://www.stn-international.de/stndatabases/details/dwpi\\_r.html](http://www.stn-international.de/stndatabases/details/dwpi_r.html) <<<  
'BIX' IS DEFAULT SEARCH FIELD FOR 'WPIX' FILE

=> d que nos L252

L242	970	SEA	FILE=WPIX	ABB=ON	PLU=ON	B14-F02B1/MC
L243	882	SEA	FILE=WPIX	ABB=ON	PLU=ON	B12-F05A/MC
L244	16	SEA	FILE=WPIX	ABB=ON	PLU=ON	C14-F02B1/MC
L245	27	SEA	FILE=WPIX	ABB=ON	PLU=ON	C12-F05A/MC
L246	1852	SEA	FILE=WPIX	ABB=ON	PLU=ON	(L242 OR L243 OR L244 OR L245)
L247	3767	SEA	FILE=WPIX	ABB=ON	PLU=ON	B12-M02D/MC
L248	4457	SEA	FILE=WPIX	ABB=ON	PLU=ON	B12-M02F/MC
L249	278	SEA	FILE=WPIX	ABB=ON	PLU=ON	C12-M02F/MC
L250	209	SEA	FILE=WPIX	ABB=ON	PLU=ON	C12-M02D/MC
L251	7446	SEA	FILE=WPIX	ABB=ON	PLU=ON	(L247 OR L248 OR L249 OR L250)
L252	16	SEA	FILE=WPIX	ABB=ON	PLU=ON	L246 AND L251

see attached  
page for  
code descriptions

=> s L252 not L256

L263 14 L252 NOT L256

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=> => dup rem L258 L259 L260 L261 L262 L263

FILE 'HCAPLUS' ENTERED AT 15:00:01 ON 07 JUL 2006

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PROCESSING COMPLETED FOR L258

PROCESSING COMPLETED FOR L259

PROCESSING COMPLETED FOR L260

PROCESSING COMPLETED FOR L261

PROCESSING COMPLETED FOR L262

PROCESSING COMPLETED FOR L263

L264 63 DUP REM L258 L259 L260 L261 L262 L263 (9 DUPLICATES REMOVED)

ANSWERS '1-28' FROM FILE HCAPLUS

ANSWERS '29-39' FROM FILE MEDLINE

ANSWERS '40-49' FROM FILE EMBASE

ANSWER '50' FROM FILE BIOSIS

ANSWERS '51-52' FROM FILE DRUGU

ANSWERS '53-63' FROM FILE WPIX

=&gt; d ibib abs hitind hitstr L264 1-28; d iall L264 29-63

L264 ANSWER 1 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 3

ACCESSION NUMBER: 2002:977668 HCAPLUS

DOCUMENT NUMBER: 138:61309

TITLE: Enhanced steroidal drug delivery in transdermal systems

INVENTOR(S): Houze, David; Nguyen, Viet

PATENT ASSIGNEE(S): Noven Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 49 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002102390	A1	20021227	WO 2002-US16579	20020618
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2451043	AA	20021227	CA 2002-2451043	20020618
EP 1406633	A1	20040414	EP 2002-749537	20020618
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2002010516	A	20041005	BR 2002-10516	20020618
CN 1543349	A	20041103	CN 2002-816000	20020618
JP 2005500299	T2	20050106	JP 2003-504976	20020618
US 2003152613	A1	20030814	US 2002-330279	20021230
US 2003152614	A1	20030814	US 2002-330360	20021230
US 2003152615	A1	20030814	US 2002-330361	20021230
US 2003232073	A1	20031218	US 2002-330281	20021230
NO 2003005645	A	20040213	NO 2003-5645	20031217
PRIORITY APPLN. INFO.:			US 2001-298381P	P 20010618
			US 2001-948107	A 20010907
			WO 2002-US16579	W 20020618

AB A composition for transdermal administration resulting from an admixt. includes a therapeutically effective amount of a drug that includes a parent drug and a prodrug and a carrier, wherein the parent drug and prodrug are individually present in an amount sufficient for a pharmacol. effect. The admixt. include: a therapeutically effective amount of a steroid and a steroid derivative and a carrier for the steroid. The steroid and the corresponding derivative are present in a weight ratio of 10:1 to 1:10

steroid-corresponding steroid derivative In a preferred embodiment ratio is 6:1 to 1:6. In a preferred embodiment, the corresponding steroid derivative is a steroidal ester. In another preferred embodiment, the carrier is a polymer that includes a pressure-sensitive **adhesive**. In another preferred embodiment, the parent drug is an ACE inhibitor such as ramipril and the prodrug is an ACE inhibitor prodrug such as ramipril Et and/or Me esters. Thus, a transdermal delivery system contained norethindrone 1.2, estradiol 0.9, norethindrone acetate 2.5, VA-64 15.0, GMS-737 (acrylic PSA), oleic acid 3.0, dipropylene glycol 9.0, and Bio-PSA-7-4603 63.4%.

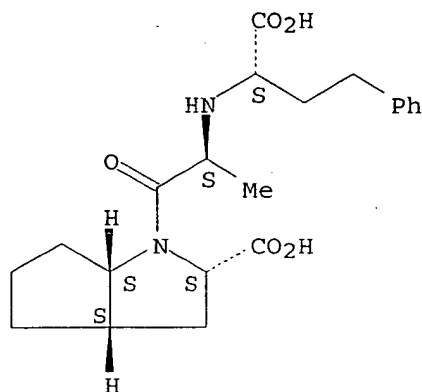
- IC ICM A61K031-56
- ICS A61K031-55; A61K031-415; A61K031-40
- CC 63-6 (Pharmaceuticals)
- Section cross-reference(s): 2
- ST steroid drug delivery transdermal; **adhesive** transdermal steroid drug delivery; estrogen delivery transdermal **adhesive**
- IT Polysiloxanes, biological studies
- RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
- (BIO-PSA 7-4102, BIO-PSA 7-4603, pressure-sensitive **adhesive**; enhanced steroidal drug delivery in transdermal systems)
- IT **Permeation enhancers**
- Skin
- (enhanced steroidal drug delivery in transdermal systems)
- IT Acrylic polymers, biological studies
- Polymers, biological studies
- RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
- (pressure-sensitive **adhesives**; enhanced steroidal drug delivery in transdermal systems)
- IT **Adhesives**
- (pressure-sensitive; enhanced steroidal drug delivery in transdermal systems)
- IT **Drug delivery systems**
- (prodrugs; enhanced steroidal drug delivery in **transdermal** systems)
- IT **Drug delivery systems**
- (**transdermal**; enhanced steroidal drug delivery in **transdermal** systems)
- IT 87269-97-4, Ramiprilat 87333-19-5, Ramipril 108313-11-7
- RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
- (**ACE inhibitor**; enhanced steroidal drug delivery in transdermal systems)
- IT 9015-82-1, **ACE**
- RL: BSU (Biological study, unclassified); BIOL (Biological study)
- (**inhibitors**; enhanced steroidal drug delivery in transdermal systems)
- IT 25086-89-9, VA 64 63450-14-6, Gelva Multipolymer Solution 788 156014-81-2, Scotchpak 1022 186597-20-6, Gelva Multipolymer Solution 737
- RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
- (pressure-sensitive **adhesive**; enhanced steroidal drug delivery in transdermal systems)
- IT 3758-34-7, Estradiol propionate
- RL: PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
- (pressure-sensitive **adhesive**; enhanced steroidal drug delivery in transdermal systems)
- IT 87269-97-4, Ramiprilat 87333-19-5, Ramipril
- RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(ACE inhibitor; enhanced steroidal drug delivery in transdermal systems)

RN 87269-97-4 HCAPLUS

CN Cyclopenta[b]pyrrole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-carboxy-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,6aS) - (9CI) (CA INDEX NAME)

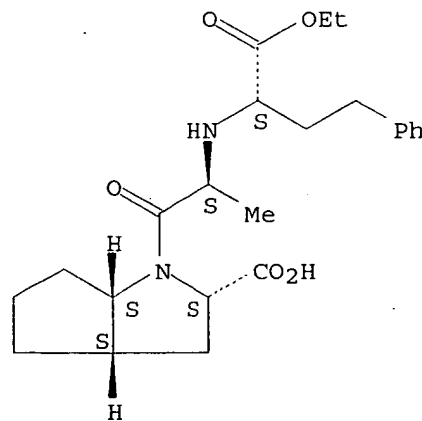
Absolute stereochemistry.



RN 87333-19-5 HCAPLUS

CN Cyclopenta[b]pyrrole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,6aS) - (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 9015-82-1, ACE

RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; enhanced steroidal drug delivery in transdermal systems)

RN 9015-82-1 HCAPLUS

CN Carboxypeptidase, dipeptidyl, A (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L264 ANSWER 2 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 6

ACCESSION NUMBER: 1993:633967 HCAPLUS

DOCUMENT NUMBER: 119:233967

TITLE: Caprylic acid **esters** as cosolvents for transdermal benazepril delivery

AUTHOR(S): Shevchuk, I.; Comfort, A.; Petrak, K.

CORPORATE SOURCE: Ciba-Geigy, Ardsley, NY, USA

SOURCE: Proc. Int. Symp. Controlled Release Bioact. Mater., 20th (1993), 428-9. Editor(s): Roseman, Theodore J.; Peppas, Nicholas A.; Gabelnick, Henry L. Controlled Release Soc.: Deerfield, Ill.  
CODEN: 59LOAL

DOCUMENT TYPE: Conference

LANGUAGE: English

AB Solns. of varying composition of caprylic acid esters (CAE) in 80/20 ethanol/water can be useful in controlling the skin permeation rate of benazepril. Since propylene glycol, the minor component of CAE, lowered the benazepril transport rate, the mono and diesters must be responsible for the 2.0-4.4-fold increase over the control. CAE in ethanol/water may be a useful solvent system for the transdermal delivery of similar ACE inhibitors such as Captopril and Enalapril. Further characterization of the CAE composition may allow for greater optimization and control of benazepril skin transport rates. The potential of this solvent system in combination with other alcs. (e.g. 1-propanol, t-butanol) or with a range of different acid esters (e.g. C4, C6, C10, C12) has not yet been investigated.

CC 63-6 (Pharmaceuticals)

ST benazepril transdermal caprylic **ester** cosolvent

IT **Pharmaceutical dosage forms**  
(transdermal, benazepril, caprylic acid **esters** as cosolvents for)

IT 124-07-2D, Caprylic acid, **esters**  
RL: BIOL (Biological study)  
(cosolvents, for transdermal delivery of benazepril)

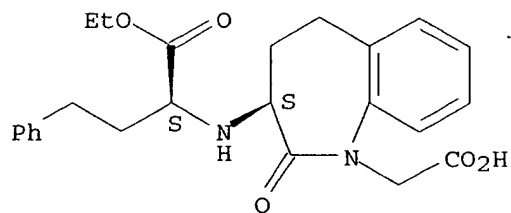
IT 86541-75-5, Benazepril  
RL: BIOL (Biological study)  
(transdermal delivery of, caprylic acid **esters** as cosolvents for)

IT 86541-75-5, Benazepril  
RL: BIOL (Biological study)  
(transdermal delivery of, caprylic acid **esters** as cosolvents for)

RN 86541-75-5 HCAPLUS

CN 1H-1-Benzazepine-1-acetic acid, 3-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-2,3,4,5-tetrahydro-2-oxo-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L264 ANSWER 3 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 7  
 ACCESSION NUMBER: . 1992:136246 HCAPLUS  
 DOCUMENT NUMBER: 116:136246  
 TITLE: Topical pharmaceutical compositions containing  
 zwitterionic drugs  
 INVENTOR(S): Mazzenga, Gerard Cesidio; Berner, Bret  
 PATENT ASSIGNEE(S): Ciba-Geigy A.-G., Switz.  
 SOURCE: Eur. Pat. Appl., 8 pp.  
 CODEN: EPXXDW  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

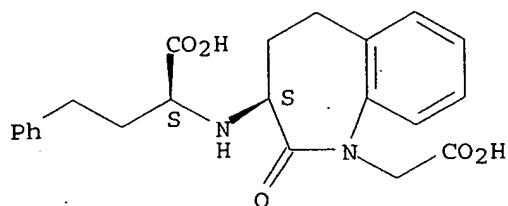
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 439430	A2	19910731	EP 1991-810040	19910117
EP 439430	A3	19910925		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
US 5073539	A	19911217	US 1990-468388	19900122
AU 9169346	A1	19910725	AU 1991-69346	19910114
CA 2034516	AA	19910723	CA 1991-2034516	19910118
ZA 9100409	A	19910925	ZA 1991-409	19910121
JP 04297417	A2	19921021	JP 1991-5805	19910122
PRIORITY APPLN. INFO.:			US 1990-468388	A 19900122
AB Topical pharmaceutical compns. containing zwitterionic drugs and methods of administering zwitterions are disclosed. The compns. comprise a zwitterionic drug in a salt form and a solvent therefor. Zwitterionic drugs have improved flux through the skin when the salt form of the zwitterion is used. Solubility of various salts of phenylalanine, baclofen, libenzapril, and benazeprilat in various solvents, in polyurethane, and in human stratum corneum are tabulated along with their permeation rate through human epidermis. Preparation of topical compns. containing benazeprilat and baclofen and nicotinic are described.				
IC	ICM A61L015-44			
	ICS A61K009-70			
CC	63-6 (Pharmaceuticals)			
IT	<b>Salts</b> , biological studies			
	RL: BIOL (Biological study)			
	(of zwitterionic compds., in transdermal pharmaceuticals)			
IT	<b>Carboxylic acids, esters</b>			
	RL: BIOL (Biological study)			
	(di-, alkyl <b>esters</b> , of zwitterionic compds., in topical pharmaceuticals)			
IT	<b>Pharmaceutical dosage forms</b>			
	(topical, of zwitterionic salts)			
IT	63-91-2, Phenylalanine, biological studies 1134-47-0, Baclofen			
	17585-69-2, Phenylalanine hydrochloride 28311-31-1, Baclofen			
	hydrochloride 53917-00-3 <b>86541-78-8</b> , Benazeprilat			
	103054-73-5 109214-55-3, Libenzapril 136670-55-8, Phenylalanine			
	hydrofluoride 136670-57-0 136670-58-1 136670-59-2 136670-60-5			
	136670-61-6 136670-64-9 136670-65-0 136670-66-1 138221-23-5			
	138221-24-6 138221-25-7 139562-12-2, Libenzapril dihydrobromide			
	RL: BIOL (Biological study)			
	(solubility and permeation of, zwitterionic salt form in topical pharmaceutical compns.)			
IT	<b>86541-78-8</b> , Benazeprilat			
	RL: BIOL (Biological study)			
	(solubility and permeation of, zwitterionic salt form in topical			

pharmaceutical compns.)

RN 86541-78-8 HCAPLUS

CN 1H-1-Benzazepine-1-acetic acid, 3-[[[(1S)-1-carboxy-3-phenylpropyl]amino]-2,3,4,5-tetrahydro-2-oxo-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L264 ANSWER 4 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 8

ACCESSION NUMBER: 1991:415608 HCAPLUS

DOCUMENT NUMBER: 115:15608

TITLE: Transdermal compositions containing absorption enhancers and resins

INVENTOR(S): Yamada, Masayuki; Nonomura, Muneo; Nishikawa, Kohei

PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan

SOURCE: Eur. Pat. Appl., 13 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 399432	A2	19901128	EP 1990-109593	19900521
EP 399432	A3	19910522		
EP 399432	B1	19940622		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
CA 2017442	AA	19901125	CA 1990-2017442	19900524
JP 03072416	A2	19910327	JP 1990-136332	19900524
US 5362497	A	19941108	US 1992-820020	19920113

PRIORITY APPLN. INFO.:		
	JP 1989-133364	A 19890525
	US 1990-524870	B1 19900518

AB A transdermal composition which has a long-lasting pharmacol. action contains a water-soluble and a fat-soluble absorption enhancer and a super water-absorbent resin. TRH was dissolved in a mixture of propylene glycol, Sumikagel SP-510 (acrylic acid ester-vinyl acetate copolymer hydrolyzate), polysorbate 80, isopropyl myristate, and water and then homogenized. The emulsion was absorbed into a rayon web of nonwoven fabric and put into a silicone chamber to provide a transdermal composition. The above transdermal

composition was

put on a clipped abdomen of rats and the plasma concentration of TRH was observed

IC ICM A61L015-16

ICS A61K047-32

CC 63-6 (Pharmaceuticals)

IT Carboxylic acids, biological studies

RL: BIOL (Biological study)

(aliphatic, C6-20, as absorption enhancers, transdermal pharmaceutical composition containing)

IT Fatty acids, esters

RL: BIOL (Biological study)  
 (long-chain, **esters**, as absorption enhancers, transdermal  
 pharmaceutical composition containing)

IT **Pharmaceutical dosage forms**  
 (transdermal, absorption enhancers and water-absorbing  
 polymers in)

IT 9015-82-1, Angiotensin converting  
 enzyme 100303-21-7  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (inhibitor, transdermal composition of, absorption enhancers and  
 water-absorbing polymers in)

IT 79-10-7D, 2-Propenoic acid, **esters**, copolymers with vinyl  
 acetate, hydrolyzed 108-05-4D, Acetic acid ethenyl **ester**,  
 copolymers with acrylic acid **esters**, hydrolyzed  
 RL: BIOL (Biological study)  
 (transdermal composition containing, as water absorbent)

IT 9015-82-1, Angiotensin converting  
 enzyme  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (inhibitor, transdermal composition of, absorption enhancers and  
 water-absorbing polymers in)

RN 9015-82-1 HCAPLUS  
 CN Carboxypeptidase, dipeptidyl, A (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

L264 ANSWER 5 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:340945 HCAPLUS

DOCUMENT NUMBER: 144:398323

TITLE: Transdermal drug delivery device containing polymeric  
 backing layer

INVENTOR(S): Kanios, David; Mantelle, Juan A.; Nguyen, Viet

PATENT ASSIGNEE(S): Noven Pharmaceuticals, Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 28 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006078604	A1	20060413	US 2005-245180	20051007
WO 2006044206	A2	20060427	WO 2005-US35806	20051007
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRIORITY APPLN. INFO.: US 2004-616861P P 20041008

AB A transdermal drug delivery system for the topical application of one or  
 more active agents contained in one or more polymeric and/or adhesive  
 carrier layers, proximate to a non-drug containing polymeric backing layer

which can control the delivery rate and profile of the transdermal drug delivery system by adjusting the moisture vapor transmission rate of the polymeric backing layer. Thus, backing layer comprising polyester and ethylene vinyl acetate was used. The backing layer (Scotchpak 9732) had a moisture vapor transmission rate of 15.5 g/ m<sup>2</sup>/24 h. The matrix blend which included 7 % by weight clonidine, 83 % by weight of a nonfunctional, acrylic-based pressure sensitive adhesive (DuroTak 73-9301) and 10 % by weight of a carboxy functional acrylic-based pressure sensitive adhesive (DuroTak 87-2852) was formed over the backing layer.

INCL 424449000

CC 63-6 (Pharmaceuticals)

IT **Medical goods**

(adhesives; transdermal drug delivery device containing polymeric backing layer)

IT **Drug delivery systems**

(topical; transdermal drug delivery device containing polymeric backing layer)

IT **Drug delivery systems**

(transdermal; transdermal drug delivery device containing polymeric backing layer)

IT 50-03-3, Corticaine 50-28-2, Estradiol, biological studies 50-47-5, Desipramine 50-49-7, Imipramine 51-34-3, Scopolamine 51-64-9 52-86-8, Haloperidol 54-11-5, Nicotine 55-63-0, Nitroglycerin 58-18-4, Methyl testosterone 58-22-0, Testosterone 60-56-0, Methimazole 72-69-5 79-10-7D, Acrylic acid, polymer 86-21-5, Pheniramine 92-13-7, Pilocarpine 94-09-7, Benzocaine 94-25-7, Butamben 100-42-5D, Styrene, polymer 106-99-0D, Butadiene, polymer 107-13-1, Acrylonitrile, biological studies 108-05-4, Vinyl acetate, biological studies 113-45-1, Methyl phenidate 122-09-8, Phentermine 132-22-9, Chlorophenamine 137-58-6, Lidocaine 149-16-6, Butacaine 156-34-3 300-62-9, Amphetamine 303-53-7, Cyclobenzaprine 466-99-9, Hydromorphone 537-46-2, Methamphetamine 721-50-6, Prilocaine 1225-55-4, Protriptyline hydrochloride 1622-61-3, Clonazepam 1668-19-5, Doxepin 3785-21-5, Butanilicaine 4205-90-7, Clonidine 9002-85-1, Polyvinylidene chloride 9002-86-2, Polyvinyl chloride 9002-88-4, Polyethylene 9002-89-5, Polyvinyl alcohol 9003-07-0, Polypropylene 9003-19-4, Polyvinyl ether 9003-27-4, Polyisobutylene 9003-29-6, Polybutylene 9003-31-0, Polyisoprene 9003-53-6, Polystyrene 9003-55-8, Styrene/butadiene polymer 9004-35-7 19982-08-2, Memantine 22071-15-4, Ketoprofen 24937-78-8, Ethylene/vinyl acetate copolymer 25067-34-9, Ethylene vinyl alcohol copolymer 25103-74-6, Ethylene-methyl acrylate copolymer 28981-97-7, Alprazolam 34911-55-2, Bupropion 54910-89-3, Fluoxetine 58581-89-8, Azelastine 61869-08-7, Paroxetine 62571-86-2, Captopril 66722-44-9, Bisoprolol 75847-73-3, Enalapril 79794-75-5, Loratadine 87333-19-5, Ramipril 91374-21-9, Ropinirole 104632-26-0, Pramipexole 105729-79-1, Isoprene-styrene block copolymer 116539-59-4, Duloxetine 158747-02-5, Frovatriptan 162731-15-9, DuroTak 87-2852 671241-40-0, Scotchpak 9732 882695-71-8, Duro-Tak 73-9301

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(transdermal drug delivery device containing polymeric backing layer)

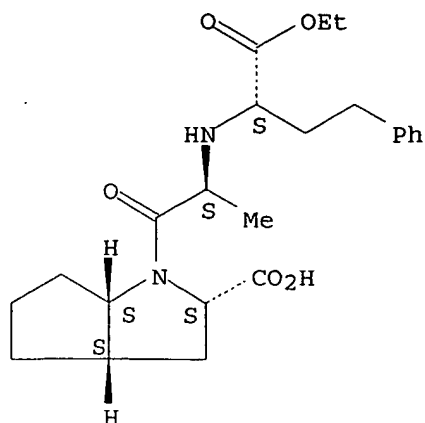
IT 87333-19-5, Ramipril

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(transdermal drug delivery device containing polymeric backing layer)

RN 87333-19-5 HCAPLUS

CN Cyclopenta[b]pyrrole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,6aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L264 ANSWER 6 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1021642 HCAPLUS

DOCUMENT NUMBER: 143:311996

TITLE: Methods for inhibiting platelet activation and aggregation, and therapeutic uses for conditions or surgical procedures that may result in unwanted platelet aggregation

INVENTOR(S): Porter, Stephen R.; Flaharty, Kristen K.; Tcheng, James E.; Ferkany, John W.

PATENT ASSIGNEE(S): Vddi Pharmaceuticals, USA

SOURCE: PCT Int. Appl., 50 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005087266	A1	20050922	WO 2005-US7440	20050307
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 2004-550792P P 20040305

AB The invention features methods for preventing platelet activation and aggregation and for treating individuals suffering from conditions or undergoing procedures that may result in unwanted platelet aggregation. The methods are based on the i.v., s.c., or transdermal administration of a platelet activation or aggregation inhibitor, e.g., xemilofiban, followed by oral administration of the same or a different platelet activation or aggregation inhibitor. The treatment may commence prior to a medical or surgical procedure or after the outbreak of an adverse medical condition, either of which results in the activation of platelets

that may lead to thrombus formation, and may continue thereafter.

IC ICM A61K039-42  
ICS A61K038-00; A61K031-70; A61K031-727; A61K031-60; A61K031-519;  
A61K031-44; A61K031-445; A61K031-40; A61K031-24

CC 63-6 (Pharmaceuticals)

IT **Drug delivery systems**  
(injections, **transdermal**; combination therapy for inhibition  
of platelet aggregation)

IT Drug delivery systems  
(**patch**; combination therapy for inhibition of platelet  
aggregation)

IT 9002-05-5, Factor Xa 9015-82-1, **Angiotensin  
converting enzyme** 39391-18-9, Cyclooxygenase  
50812-31-2  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(**inhibitor**; combination therapy for **inhibition** of  
platelet aggregation)

IT 9015-82-1, **Angiotensin converting  
enzyme**  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(**inhibitor**; combination therapy for **inhibition** of  
platelet aggregation)

RN 9015-82-1 HCAPLUS

CN Carboxypeptidase, dipeptidyl, A (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L264 ANSWER 7 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:732585 HCAPLUS

DOCUMENT NUMBER: 143:179169

TITLE: Cosmetic compositions **ACE inhibitors**  
and/or angiotensin II receptor antagonists for  
treatment of skin aging

INVENTOR(S): Jensen, Benny Vittrup

PATENT ASSIGNEE(S): Ace Aps, Den.

SOURCE: PCT Int. Appl., 48 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005072696	A1	20050811	WO 2005-DK65	20050128
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.: DK 2004-136 A 20040130  
US 2004-553661P P 20040316

- AB The present invention relates to a method and cosmetic preparation comprising an ACE inhibitor and/or angiotensin II receptor antagonist present in an amount of about 0.01 to 100 mg/kg each for the treatment of skin aging or wrinkling. For example, an ACE inhibitor, such as lisinopril 10 mg/kg was formulated in a cream base comprising (i) Phase A containing Emulgade SE 4.0%, Cutina MD 1.0%, Lanette O 1.0%, Baysilon M 350 0.5%, Cetirol PGL 7.0%, Cetirol OE 4.0%, and Copherol 1250 0.5%, (ii) Phase B containing D-panthenol 1.0%, glycerin (86%) 5.0%, and water 71.5%, (iii) Phase C containing Carbopol 980 0.2% and Cetirol PGL 1.0%, and (iv) Phase C containing KOH (20%) 0.3% and perfume/preservative as needed.
- IC ICM A61K007-48
- CC 62-4 (Essential Oils and Cosmetics)  
Section cross-reference(s): 63
- ST **ACE inhibitor** angiotensin receptor antagonist cosmetic skin aging
- IT Skin, disease  
(Kindler syndrome, associated with aging or wrinkling; compns. containing **ACE inhibitors** and/or angiotensin II receptor antagonists for improvement and maintenance of skin tone and treatment of skin aging)
- IT Acne  
Eczema  
Psoriasis  
(agents for treatment of; compns. containing **ACE inhibitors** and/or angiotensin II receptor antagonists for improvement and maintenance of skin tone and treatment of skin aging)
- IT Skin, disease  
(aging, wrinkles; compns. containing **ACE inhibitors** and/or angiotensin II receptor antagonists for improvement and maintenance of skin tone and treatment of skin aging)
- IT Angiotensin receptor antagonists  
(angiotensin II; compns. containing **ACE inhibitors** and/or angiotensin II receptor antagonists for improvement and maintenance of skin tone and treatment of skin aging)
- IT Cosmetics  
(antiaging; compns. containing **ACE inhibitors** and/or angiotensin II receptor antagonists for improvement and maintenance of skin tone and treatment of skin aging)
- IT Anti-inflammatory agents  
Antimicrobial agents  
Antioxidants  
Antitumor agents  
Antiviral agents  
Bleaching agents  
Chelating agents  
Fungicides  
Humectants  
Insect repellents  
Pigments, nonbiological  
Preservatives  
Radical scavengers  
Skin preparations (pharmaceutical)  
Sunscreens  
Suntanning agents  
Whitening agents  
(compns. containing **ACE inhibitors** and/or angiotensin II receptor antagonists for improvement and maintenance of skin tone and treatment of skin aging)
- IT Amino acids, biological studies  
Biopolymers

Lipids, biological studies  
Nucleic acids  
Peptides, biological studies  
Peroxides, biological studies  
Polymers, biological studies  
Proteins  
Retinoids  
Salts, biological studies  
Vitamins  
RL: COS (Cosmetic use); BIOL (Biological study); USES (Uses)  
(compns. containing **ACE inhibitors** and/or angiotensin  
II receptor antagonists for improvement and maintenance of skin tone  
and treatment of skin aging)  
IT Hormones, animal, biological studies  
RL: COS (Cosmetic use); THU (Therapeutic use); BIOL (Biological study);  
USES (Uses)  
(compns. containing **ACE inhibitors** and/or angiotensin  
II receptor antagonists for improvement and maintenance of skin tone  
and treatment of skin aging)  
IT Cosmetics  
(creams; compns. containing **ACE inhibitors** and/or  
angiotensin II receptor antagonists for improvement and maintenance of  
skin tone and treatment of skin aging)  
IT Cosmetics  
(depilatories; compns. containing **ACE inhibitors** and/or  
angiotensin II receptor antagonists for improvement and maintenance of  
skin tone and treatment of skin aging)  
IT Cosmetics  
(emollients; compns. containing **ACE inhibitors** and/or  
angiotensin II receptor antagonists for improvement and maintenance of  
skin tone and treatment of skin aging)  
IT Saccharum officinarum  
(extract; compns. containing **ACE inhibitors** and/or  
angiotensin II receptor antagonists for improvement and maintenance of  
skin tone and treatment of skin aging)  
IT Embryophyta  
Plants  
(exts.; compns. containing **ACE inhibitors** and/or  
angiotensin II receptor antagonists for improvement and maintenance of  
skin tone and treatment of skin aging)  
IT Cosmetics  
(face packs; compns. containing **ACE inhibitors** and/or  
angiotensin II receptor antagonists for improvement and maintenance of  
skin tone and treatment of skin aging)  
IT Hair preparations  
(growth stimulants; compns. containing **ACE inhibitors**  
and/or angiotensin II receptor antagonists for improvement and  
maintenance of skin tone and treatment of skin aging)  
IT Vein, disease  
(hemorrhoid, agents for treatment of; compns. containing **ACE**  
**inhibitors** and/or angiotensin II receptor antagonists for  
improvement and maintenance of skin tone and treatment of skin aging)  
IT Carboxylic acids, biological studies  
RL: COS (Cosmetic use); BIOL (Biological study); USES (Uses)  
(hydroxy; compns. containing **ACE inhibitors** and/or  
angiotensin II receptor antagonists for improvement and maintenance of  
skin tone and treatment of skin aging)  
IT Corticosteroids, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(hypersecretion, skin aging or wrinkling associated with; compns. containing

**ACE inhibitors** and/or angiotensin II receptor antagonists for improvement and maintenance of skin tone and treatment of skin aging)

- IT Cosmetics  
(lipsticks; compns. containing **ACE inhibitors** and/or angiotensin II receptor antagonists for improvement and maintenance of skin tone and treatment of skin aging)
- IT Cosmetics  
Drug delivery systems  
(liqs.; compns. containing **ACE inhibitors** and/or angiotensin II receptor antagonists for improvement and maintenance of skin tone and treatment of skin aging)
- IT Cosmetics  
(lotions; compns. containing **ACE inhibitors** and/or angiotensin II receptor antagonists for improvement and maintenance of skin tone and treatment of skin aging)
- IT Cosmetics  
(makeup removers; compns. containing **ACE inhibitors** and/or angiotensin II receptor antagonists for improvement and maintenance of skin tone and treatment of skin aging)
- IT Cosmetics  
(makeups; compns. containing **ACE inhibitors** and/or angiotensin II receptor antagonists for improvement and maintenance of skin tone and treatment of skin aging)
- IT Metabolic disorders  
(metabolic syndrome X, skin aging or wrinkling associated with; compns. containing **ACE inhibitors** and/or angiotensin II receptor antagonists for improvement and maintenance of skin tone and treatment of skin aging)
- IT Collagens, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(modulators and synthesis enhancers; compns. containing **ACE inhibitors** and/or angiotensin II receptor antagonists for improvement and maintenance of skin tone and treatment of skin aging)
- IT Cosmetics  
(moisturizers; compns. containing **ACE inhibitors** and/or angiotensin II receptor antagonists for improvement and maintenance of skin tone and treatment of skin aging)
- IT Drug delivery systems  
(ointments, creams; compns. containing **ACE inhibitors** and/or angiotensin II receptor antagonists for improvement and maintenance of skin tone and treatment of skin aging)
- IT Drug delivery systems  
(ointments; compns. containing **ACE inhibitors** and/or angiotensin II receptor antagonists for improvement and maintenance of skin tone and treatment of skin aging)
- IT Carboxylic acids, biological studies  
RL: COS (Cosmetic use); BIOL (Biological study); USES (Uses)  
(oxo; compns. containing **ACE inhibitors** and/or angiotensin II receptor antagonists for improvement and maintenance of skin tone and treatment of skin aging)
- IT Drug delivery systems  
(pastes; compns. containing **ACE inhibitors** and/or angiotensin II receptor antagonists for improvement and maintenance of skin tone and treatment of skin aging)
- IT Cosmetics  
(patches; compns. containing **ACE inhibitors** and/or angiotensin II receptor antagonists for improvement and maintenance of skin tone and treatment of skin aging)
- IT Skin, disease

- (photoaging; compns. containing **ACE inhibitors** and/or angiotensin II receptor antagonists for improvement and maintenance of skin tone and treatment of skin aging)
- IT Cosmetics  
(powders; compns. containing **ACE inhibitors** and/or angiotensin II receptor antagonists for improvement and maintenance of skin tone and treatment of skin aging)
- IT Aging, animal  
(progeria, skin aging or wrinkling associated with; compns. containing **ACE inhibitors** and/or angiotensin II receptor antagonists for improvement and maintenance of skin tone and treatment of skin aging)
- IT Glucocorticoids  
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
(skin aging or wrinkling associated with administration of; compns. containing **ACE inhibitors** and/or angiotensin II receptor antagonists for improvement and maintenance of skin tone and treatment of skin aging)
- IT Diabetes mellitus  
Tobacco smoke  
Werner syndrome  
(skin aging or wrinkling associated with; compns. containing **ACE inhibitors** and/or angiotensin II receptor antagonists for improvement and maintenance of skin tone and treatment of skin aging)
- IT Drug delivery systems  
(sprays; compns. containing **ACE inhibitors** and/or angiotensin II receptor antagonists for improvement and maintenance of skin tone and treatment of skin aging)
- IT Decorins  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(synthesis enhancers; compns. containing **ACE inhibitors** and/or angiotensin II receptor antagonists for improvement and maintenance of skin tone and treatment of skin aging)
- IT Drug delivery systems  
(topical; compns. containing **ACE inhibitors** and/or angiotensin II receptor antagonists for improvement and maintenance of skin tone and treatment of skin aging)
- IT Drug delivery systems  
(transdermal; compns. containing **ACE inhibitors** and/or angiotensin II receptor antagonists for improvement and maintenance of skin tone and treatment of skin aging)
- IT Cosmetics  
(wrinkle-preventing; compns. containing **ACE inhibitors** and/or angiotensin II receptor antagonists for improvement and maintenance of skin tone and treatment of skin aging)
- IT 145040-37-5, Candesartan cilexetil  
RL: COS (Cosmetic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(Atacand; compns. containing **ACE inhibitors** and/or angiotensin II receptor antagonists for improvement and maintenance of skin tone and treatment of skin aging)
- IT 138402-11-6, Avapro  
RL: COS (Cosmetic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(Irbesartan; compns. containing **ACE inhibitors** and/or angiotensin II receptor antagonists for improvement and maintenance of skin tone and treatment of skin aging)
- IT 144701-48-4, Micardis  
RL: COS (Cosmetic use); THU (Therapeutic use); BIOL (Biological study);

## USES (Uses)

(Telmisartan; compns. containing **ACE inhibitors** and/or angiotensin II receptor antagonists for improvement and maintenance of skin tone and treatment of skin aging)

IT 137862-53-4, Diovan

RL: COS (Cosmetic use); THU (Therapeutic use); BIOL (Biological study);  
USES (Uses)

(Valsartan; compns. containing **ACE inhibitors** and/or angiotensin II receptor antagonists for improvement and maintenance of skin tone and treatment of skin aging)

IT 50-21-5, Lactic acid, biological studies 77-92-9, Citric acid, biological studies 79-14-1, Hydroxyethanoic acid, biological studies 87-69-4, Tartaric acid, biological studies 116-31-4, Retinal 302-79-4, Retinoic acid 506-26-3,  $\gamma$ -Linolenic acid 600-15-7, 2-Hydroxybutanoic acid 6915-15-7, Malic acid 7235-40-7,  $\beta$ -Carotene 7440-66-6, Zinc, biological studies 7782-49-2, Selenium, biological studies 92348-62-4, Hydroxycaprylic acid  
RL: COS (Cosmetic use); BIOL (Biological study); USES (Uses)

(compns. containing **ACE inhibitors** and/or angiotensin II receptor antagonists for improvement and maintenance of skin tone and treatment of skin aging)

IT 62571-86-2, Captopril 74258-86-9, Alacepril 75695-93-1, Isradipin 75847-73-3, Enalapril 76547-98-3, Lisinopril 81872-10-8, Zofenopril 82834-16-0, Perindopril 83435-66-9, Delapril 83647-97-6, Spirapril 85441-61-8, Quinapril 86541-75-5, Benazepril 87333-19-5, Ramipril 87679-37-6, Trandolapril 88768-40-5, Cilazapril 89371-37-9, Imidapril 98048-97-6, Fosinopril 103775-10-6, Moexipril 111902-57-9, Temocapril 114798-26-4, Losartan 124750-99-8, Cozaar 133040-01-4, Eprosartan 139481-59-7, Candesartan 145733-36-4, Tasosartan 145781-32-4, Zolasartan

RL: COS (Cosmetic use); THU (Therapeutic use); BIOL (Biological study);  
USES (Uses)

(compns. containing **ACE inhibitors** and/or angiotensin II receptor antagonists for improvement and maintenance of skin tone and treatment of skin aging)

IT 9015-82-1 141907-41-7

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(**inhibitors**; compns. containing **ACE inhibitors** and/or angiotensin II receptor antagonists for improvement and maintenance of skin tone and treatment of skin aging)

IT 1406-16-2, Vitamin D

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
(skin aging or wrinkling associated with administration of; compns.

containing

**ACE inhibitors** and/or angiotensin II receptor antagonists for improvement and maintenance of skin tone and treatment of skin aging)

IT 82834-16-0, Perindopril 83647-97-6, Spirapril 86541-75-5, Benazepril 87333-19-5, Ramipril 87679-37-6, Trandolapril 88768-40-5, Cilazapril 89371-37-9, Imidapril 98048-97-6, Fosinopril 103775-10-6, Moexipril

RL: COS (Cosmetic use); THU (Therapeutic use); BIOL (Biological study);  
USES (Uses)

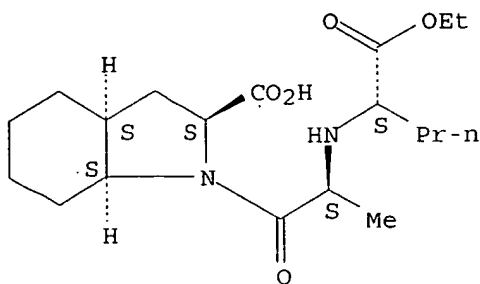
(compns. containing **ACE inhibitors** and/or angiotensin II receptor antagonists for improvement and maintenance of skin tone and treatment of skin aging)

RN 82834-16-0 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[(1S)-1-

(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI)  
(CA INDEX NAME)

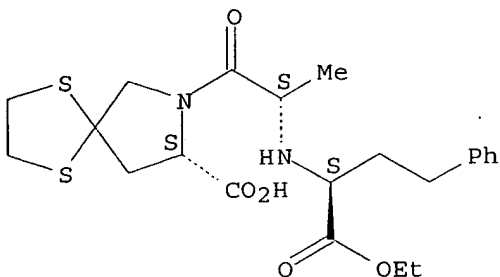
Absolute stereochemistry. Rotation (-).



RN 83647-97-6 HCAPLUS

CN 1,4-Dithia-7-azaspiro[4.4]nonane-8-carboxylic acid, 7-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-, (8S)- (9CI) (CA INDEX NAME)

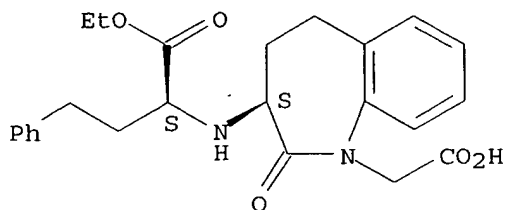
Absolute stereochemistry. Rotation (-).



RN 86541-75-5 HCAPLUS

CN 1H-1-Benzazepine-1-acetic acid, 3-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-2,3,4,5-tetrahydro-2-oxo-, (3S)- (9CI) (CA INDEX NAME)

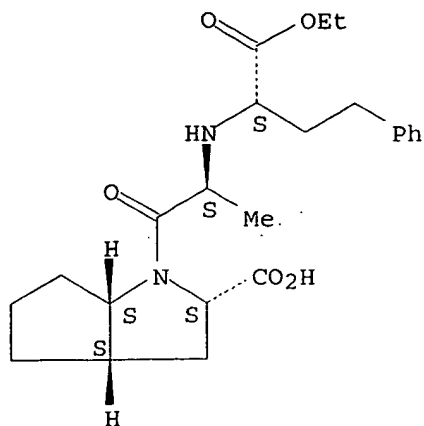
Absolute stereochemistry.



RN 87333-19-5 HCAPLUS

CN Cyclopenta[b]pyrrole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,6aS)- (9CI) (CA INDEX NAME)

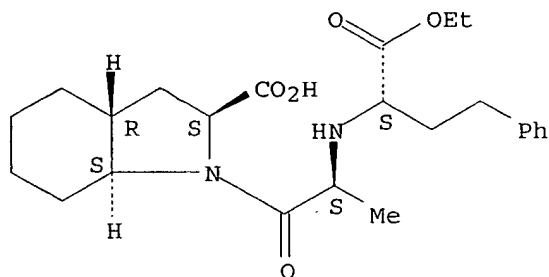
Absolute stereochemistry.



RN 87679-37-6 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aR,7aS)- (9CI) (CA INDEX NAME)

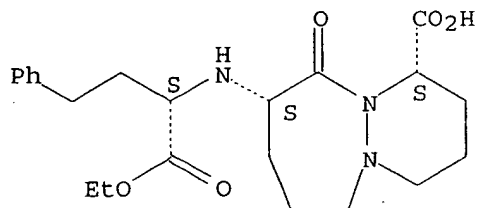
Absolute stereochemistry. Rotation (-).



RN 88768-40-5 HCAPLUS

CN 6H-Pyridazino[1,2-a][1,2]diazepine-1-carboxylic acid, 9-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]octahydro-10-oxo-, (1S,9S)- (9CI) (CA INDEX NAME)

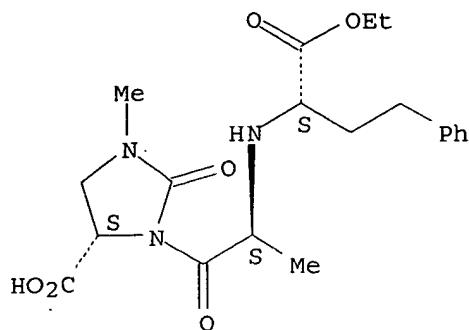
Absolute stereochemistry.



RN 89371-37-9 HCAPLUS

CN 4-Imidazolidinecarboxylic acid, 3-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1-methyl-2-oxo-, (4S)- (9CI) (CA INDEX NAME)

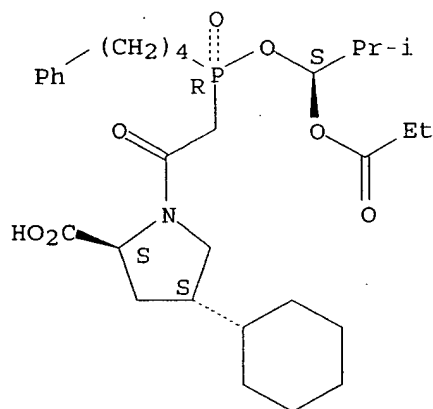
Absolute stereochemistry.



RN 98048-97-6 HCAPLUS

CN L-Proline, 4-cyclohexyl-1-[[[(R)-[(1S)-2-methyl-1-(1-oxopropoxy)propoxy] (4-phenylbutyl)phosphinyl]acetyl]-, (4S)- (9CI) (CA INDEX NAME)

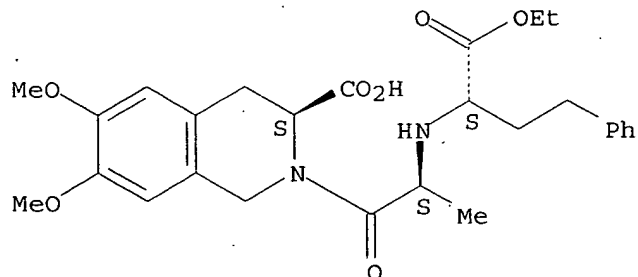
Absolute stereochemistry.



RN 103775-10-6 HCAPLUS

CN 3-Isoquinolinecarboxylic acid, 2-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-6,7-dimethoxy-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 9015-82-1

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibitors; compns. containing ACE inhibitors  
and/or angiotensin II receptor antagonists for improvement and

maintenance of skin tone and treatment of skin aging)

RN 9015-82-1 HCAPLUS

CN Carboxypeptidase, dipeptidyl, A (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L264 ANSWER 8 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:303189 HCAPLUS

DOCUMENT NUMBER: 142:309962

TITLE: Use of vitamin Ds to down regulate the  
renin-angiotensin-aldosterone system

INVENTOR(S): Melnick, Joel; Tian, Jin

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 7 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005074488	A1	20050407	US 2004-900418	20040727
PRIORITY APPLN. INFO.:			US 2003-490478P	P 20030728
AB	The invention relates to the use of Vitamin D, preferably paricalcitol, to treat, prevent and delay disease progression of diseases associated with over activation of the renin-angiotensin aldosterone system.			
IC	ICM A61K031-59			
	ICS A61K009-70			
INCL	424449000; 514167000			
CC	1-12 (Pharmacology)			
	Section cross-reference(s): 2, 63			
IT	<b>Drug delivery systems</b> (transdermal, patch; vitamin D and vitamin D analogs for down regulation of renin-angiotensin-aldosterone system)			
IT	<b>9015-82-1</b> RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; vitamin D and vitamin D analogs for down regulation of renin-angiotensin-aldosterone system)			
IT	<b>9015-82-1</b> RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors; vitamin D and vitamin D analogs for down regulation of renin-angiotensin-aldosterone system)			
RN	9015-82-1 HCAPLUS			
CN	Carboxypeptidase, dipeptidyl, A (9CI) (CA INDEX NAME)			

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

L264 ANSWER 9 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:303188 HCAPLUS

DOCUMENT NUMBER: 142:360863

TITLE: Transdermal and topical administration of drugs using  
basic permeation enhancers

INVENTOR(S): Hsu, Tsung-Min; Gricenko, Nicole T.; Hickey, Alan T.  
J.; Jacobson, Eric C.; Lobello, Rose C.; Obara, Jane;  
Luo, Eric C.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 47 pp., Cont.-in-part of Ser.

No. US 2003-675603, filed on 29 Sep 2003 which is  
CODEN: USXXCO

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 26

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005074487	A1	20050407	US 2004-863432	20040607
US 2001051166	A1	20011213	US 2000-738410	20001214
US 6586000	B2	20030701		
US 2002018803	A1	20020214	US 2000-738395	20001214
US 6719997	B2	20040413		
US 2002034554	A1	20020321	US 2001-972008	20011004
US 6582724	B2	20030624		
ZA 2002004671	A	20030611	ZA 2002-4671	20020611
US 2002192300	A1	20021219	US 2002-175681	20020619
US 2002192301	A1	20021219	US 2002-175682	20020619
US 2002192242	A1	20021219	US 2002-175721	20020619
US 2002192302	A1	20021219	US 2002-175769	20020619
US 2002192243	A1	20021219	US 2002-176264	20020619
US 2002197284	A1	20021226	US 2002-176265	20020619
US 6673363	B2	20040106		
US 2003124176	A1	20030703	US 2002-176952	20020621
US 2004086556	A1	20040506	US 2003-675603	20030929

PRIORITY APPLN. INFO.:

US 1999-465098	B2	19991216
US 2000-569889	B2	20000511
US 2000-607892	B2	20000630
US 2000-738395	A2	20001214
US 2000-738410	A2	20001214
US 2001-972008	A2	20011004
US 2002-175681	A2	20020619
US 2002-175682	A2	20020619
US 2002-175721	B2	20020619
US 2002-175769	B2	20020619
US 2002-176264	A2	20020619
US 2002-176265	A3	20020619
US 2002-176952	B2	20020621
US 2003-675603	A2	20030929

AB Methods are provided for enhancing the permeability of skin or mucosal tissue to topical or transdermal application of pharmacol. or cosmeceutically active agents. The methods entail the use of a base in order to increase the flux of the active agent through a body surface while minimizing the likelihood of skin damage, irritation or sensitization. The permeation enhancer can be an inorg. or organic base. Compns. and transdermal systems are also described. For example, an in vitro skin permeation of estradiol from a transdermal system containing (on dried weight) estradiol 2.6%, NaOH 1.3%, and polyisobutylene **adhesive** 96.2% provided about 20-fold more estradiol flux than in the absence of NaOH.

IC ICM A61L015-16

ICS A61K033-00

INCL 424448000; 424722000

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1, 2, 62

IT Antidepressants

Antihypertensives

Antipsychotics

Mucous membrane

**Permeation enhancers****Skin**

(basic permeation enhancers for transdermal and topical administration of drugs)

**IT Drug delivery systems**

(gels; basic permeation enhancers for **transdermal** and topical administration of drugs)

**IT Drug delivery systems**

(lotions; basic permeation enhancers for **transdermal** and topical administration of drugs)

**IT Drug delivery systems**

(ointments, creams; basic permeation enhancers for **transdermal** and topical administration of drugs)

**IT Drug delivery systems**

(ointments; basic permeation enhancers for **transdermal** and topical administration of drugs)

**IT Drug delivery systems**

(pastes; basic permeation enhancers for **transdermal** and topical administration of drugs)

**IT Drug delivery systems**

(solns.; basic permeation enhancers for **transdermal** and topical administration of drugs)

**IT Drug delivery systems**

(topical; basic permeation enhancers for **transdermal** and topical administration of drugs)

**IT Drug delivery systems**

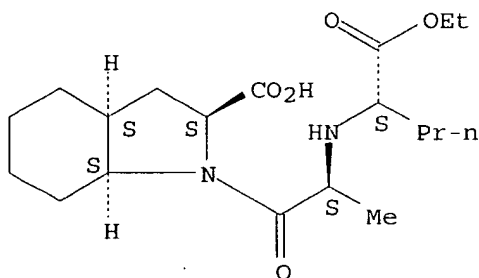
(**transdermal**; basic permeation enhancers for **transdermal** and topical administration of drugs)

**IT** 50-48-6, Amitriptyline 50-53-3, Chlorpromazine, biological studies  
 51-71-8, Phenelzine 52-86-8, Haloperidol 58-25-3, Chlorodiazepoxide  
 58-38-8, Prochlorperazine 58-39-9, Perphenazine 59-96-1,  
 Phenoxybenzamine 69-23-8, Fluphenazine 117-89-5, Trifluoroperazine  
 127-08-2, Potassium acetate 127-09-3, Sodium acetate 144-55-8, Sodium  
 bicarbonate, biological studies 155-09-9, Tranylcypromine 298-14-6,  
 Potassium bicarbonate 438-60-8, Protriptyline 497-19-8, Sodium  
 carbonate, biological studies 584-08-7, Potassium carbonate 866-84-2,  
 Potassium citrate 1305-62-0, Calcium hydroxide, biological studies  
 1305-78-8, Calcium oxide, biological studies 1309-42-8, Magnesium  
 hydroxide 1309-48-4, Magnesium oxide, biological studies 1310-58-3,  
 Potassium hydroxide, biological studies 1310-73-2, Sodium hydroxide,  
 biological studies 1336-21-6, Ammonium hydroxide 1668-19-5, Doxepin  
 1977-10-2, Loxapine 2062-78-4, Pimozide 3313-26-6, Thiothixene  
 5588-33-0, Mesoridazine 5786-21-0, Clozapine 7601-54-9, Sodium  
 phosphate 7775-19-1, Sodium metaborate 7778-53-2, Potassium phosphate  
 10361-65-6, Ammonium phosphate 13840-56-7, Sodium borate 19216-56-9,  
 Prazosin 21829-25-4, Nifedipine 26839-75-8, Timolol 36505-84-7,  
 Buspirone 42200-33-9, Nadolol 54910-89-3, Fluoxetine 55985-32-5,  
 Nicardipine 59729-33-8, Citalopram 61869-08-7, Paroxetine  
 63590-64-7, Terazosin 66085-59-4, Nimodipine 72509-76-3, Felodipine  
 72956-09-3, Carvedilol 74191-85-8, Doxazosin 75695-93-1, Isradipine  
 75847-73-3, Enalapril 76420-72-9, Enalaprilat 76547-98-3, Lisinopril  
 79617-96-2, Sertraline 82768-85-2, Quinaprilat 82834-16-0,  
 Perindopril 85441-61-8, Quinapril 85650-52-8, Mirtazapine  
 86541-75-5, Benazepril 86541-78-8, Benazeprilat  
 87269-97-4, Ramiprilat 87333-19-5, Ramipril  
 88150-42-9, Amlodipine 93413-69-5, Venlafaxine 95153-31-4,  
 Perindoprilat 95399-71-6, Fosinoprilat 98048-97-6,  
 Fosinopril 111974-72-2, Quetiapine fumarate 132539-06-1, Olanzapine  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (basic permeation enhancers for transdermal and topical administration

of drugs)

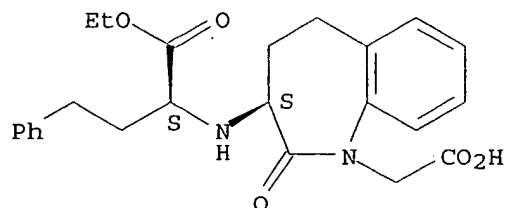
IT 82834-16-0, Perindopril 86541-75-5, Benazepril  
86541-78-8, Benazeprilat 87269-97-4, Ramiprilat  
87333-19-5, Ramipril 95153-31-4, Perindoprilat  
95399-71-6, Fosinoprilat 98048-97-6, Fosinopril  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(basic permeation enhancers for transdermal and topical administration  
of drugs)  
RN 82834-16-0 HCAPLUS  
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(  
(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



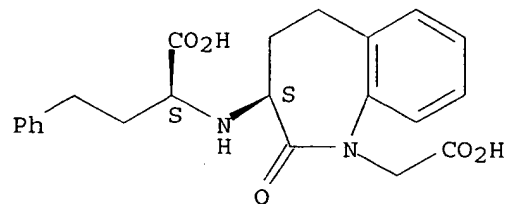
RN 86541-75-5 HCAPLUS  
CN 1H-1-Benzazepine-1-acetic acid, 3-[[[(1S)-1-(ethoxycarbonyl)-3-  
phenylpropyl]amino]-2,3,4,5-tetrahydro-2-oxo-, (3S)- (9CI) (CA INDEX  
NAME)

Absolute stereochemistry.



RN 86541-78-8 HCAPLUS  
CN 1H-1-Benzazepine-1-acetic acid, 3-[[[(1S)-1-carboxy-3-phenylpropyl]amino]-  
2,3,4,5-tetrahydro-2-oxo-, (3S)- (9CI) (CA INDEX NAME)

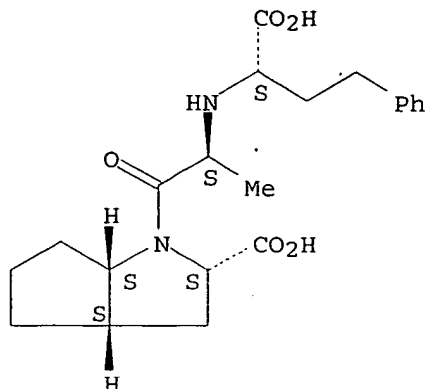
Absolute stereochemistry.



RN 87269-97-4 HCAPLUS

CN Cyclopenta[b]pyrrole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-carboxy-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,6aS)- (9CI) (CA INDEX NAME)

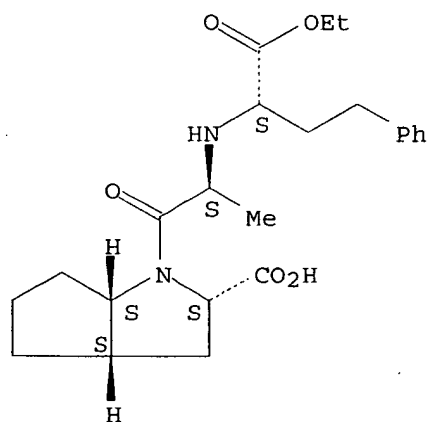
Absolute stereochemistry.



RN 87333-19-5 HCAPLUS

CN Cyclopenta[b]pyrrole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,6aS)- (9CI) (CA INDEX NAME)

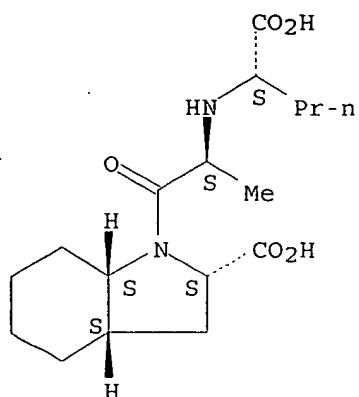
Absolute stereochemistry.



RN 95153-31-4 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-carboxybutyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI) (CA INDEX NAME)

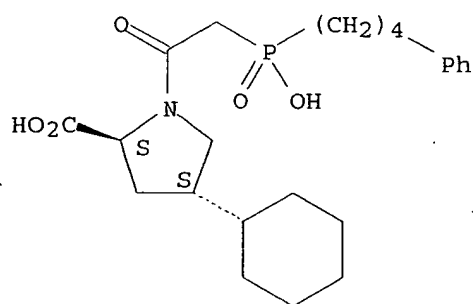
. Absolute stereochemistry.



RN 95399-71-6 HCAPLUS

CN L-Proline, 4-cyclohexyl-1-[[hydroxy(4-phenylbutyl)phosphinyl]acetyl]-,  
(4S)-(9CI) (CA INDEX NAME)

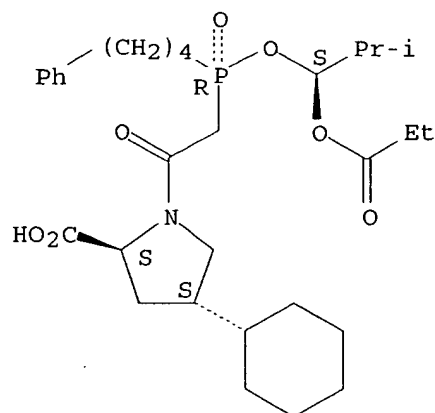
Absolute stereochemistry.



RN 98048-97-6 HCAPLUS

CN L-Proline, 4-cyclohexyl-1-[[[(R)-[(1S)-2-methyl-1-(1-oxopropoxy)propoxy](4-phenylbutyl)phosphinyl]acetyl]-, (4S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



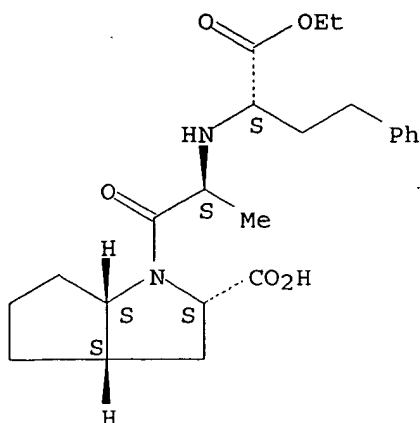
L264 ANSWER 10 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:77971 HCAPLUS  
 DOCUMENT NUMBER: 142:162654  
 TITLE: Compositions for controlling drug delivery from  
 silicone **adhesive** blends  
 INVENTOR(S): Houze, David  
 PATENT ASSIGNEE(S): Noven Pharmaceuticals, Inc., USA  
 SOURCE: U.S. Pat. Appl. Publ., 8 pp.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005019385	A1	20050127	US 2004-895688	20040721
WO 2005009417	A1	20050203	WO 2004-US23286	20040721
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1663179	A1	20060607	EP 2004-757148	20040721
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
PRIORITY APPLN. INFO.:			US 2003-488928P	P 20030721
			WO 2004-US23286	W 20040721
AB Compns. and methods for controlling transdermal drug delivery, particularly of amine-functional and basic drugs, comprising a blend of a first silicone-based polymer having a reduced silanol concentration and a second silicone-based polymer have a substantial or high silanol concentration The blend of such silicone-based polymers, particularly pressure-sensitive silicone <b>adhesives</b> , provides sufficient drug solubility and reduced initial drug delivery onset to permit a prolonged delivery duration at a substantially zero-order rate of delivery. Thus, fentanyl permeation was slowed as the silanol content of the silicone <b>adhesive</b> matrix increased.				
IC	ICM A61K009-70			
INCL	424449000			
CC	63-6 (Pharmaceuticals)			
ST	controlled release transdermal silicone <b>adhesive</b> blend			
IT	Polysiloxanes, biological studies			
	RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (BIO-PSA 7-4202 and BIO-PSA 7-4502; compns. for controlling drug delivery from silicone <b>adhesive</b> blends)			
IT	<b>Permeation enhancers</b> (compns. for controlling drug delivery from silicone <b>adhesive</b> blends)			
IT	Polymer blends RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (compns. for controlling drug delivery from silicone <b>adhesive</b> blends)			

- IT Crystallization  
(inhibitors; compns. for controlling drug delivery from silicone adhesive blends)
- IT Adhesives  
(pressure-sensitive; compns. for controlling drug delivery from silicone adhesive blends)
- IT Drug delivery systems  
(transdermal, controlled-release; compns. for controlling drug delivery from silicone adhesive blends)
- IT 61-54-1D, Triptans, derivs.  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(Triptans; compns. for controlling drug delivery from silicone adhesive blends)
- IT 50-36-2, Cocaine 50-47-5, Desipramine 50-49-7, Imipramine 50-53-3, Chlorpromazine, biological studies 51-34-3, Scopolamine 51-43-4, Epinephrine 51-55-8, Atropine, biological studies 51-64-9, DextroAmphetamine 54-11-5, Nicotine 57-27-2, Morphine, biological studies 58-22-0, Testosterone 59-46-1, Procaine 77-07-6, Levorphanol 78-44-4, Carisoprodol 94-09-7, Benzocaine 94-24-6, Tetracaine 113-45-1, Methylphenidate 122-09-8, Phentermine 137-58-6, Lidocaine 300-62-9, Amphetamine 303-53-7, Cyclobenzaprine 321-64-2, Tacrine 437-38-7, Fentanyl 466-99-9, HydroMorphine 537-46-2, MetAmphetamine 1622-61-3, Clonazepam 4205-90-7, Clonidine 5633-20-5, Oxybutynin 9003-39-8, Polyvinylpyrrolidone 9004-34-6D, Cellulose, derivs. 13523-86-9, Pindolol 25086-89-9, Vinyl acetate-vinylpyrrolidone copolymer 26839-75-8, Timolol 28981-97-7, Alprazolam 34911-55-2, Bupropion 36505-84-7, Buspirone 42200-33-9, Nadolol 52485-79-7, Buprenorphine 54910-89-3, Fluoxetine 56030-54-7, SuFentanyl 58581-89-8, Azelastine 59708-52-0, CarFentanyl 61380-40-3, LoFentanil 61869-08-7, Paroxetine 66104-22-1, Pergolide 71195-58-9, AlFentanyl 75847-73-3, Enalapril 87333-19-5, Ramipril 91374-21-9, Ropinirole 99755-59-6, Rotigotine 104632-26-0, Pramipexole 109889-09-0, Granisetron 120656-74-8, TreFentanil 132875-61-7, RemiFentanyl  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(compns. for controlling drug delivery from silicone adhesive blends)
- IT 87333-19-5, Ramipril  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(compns. for controlling drug delivery from silicone adhesive blends)
- RN 87333-19-5 HCAPLUS
- CN Cyclopenta[b]pyrrole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,6aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L264 ANSWER 11 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:26250 HCAPLUS

DOCUMENT NUMBER: 144:239892

TITLE: **Patch** for controlled transdermal delivery of drug compositions for treating hypertension, and method for preparing the same

INVENTOR(S): Wang, Rui; Yun, Liuhong; Zhou, Xiaoqing; Wang, Wengang; Chai, Dong; Duan, Lanbo; Liu, Zhongchun

PATENT ASSIGNEE(S): General Hospital of PLA, Peop. Rep. China

SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 18 pp.

CODEN: CNXXEV

DOCUMENT TYPE: Patent

LANGUAGE: Chinese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1633994	A	20050706	CN 2004-10086853	20041104
PRIORITY APPLN. INFO.:			CN 2004-10086853	20041104

AB This invention relates to a **patch** for controlled transdermal delivery of drug compns. for treating hypertension, and method for preparing the same. The **patch** comprises, in an integrally laminated manner, a substrate layer, a contact adhesive skeleton type drug reservoir layer, and a protective membrane. The drug reservoir layer contains a drug composition composed of any two kinds of drugs selected from the following classes of drugs for treating hypertension: diuretics; central  $\alpha$ -agonists and peripheral  $\alpha$ -blockers;  $\beta$ -blockers; calcium antagonists; and drugs that affect the formation of angiotensin II. A stable blood drug level can be quickly reached after one-time administration by applying the **patch** once on the chest or in the postauricular area and can be maintained in a constant, persistent, and controllable level. By this means, the peak-and-valley feature of the blood drug level resulted from oral administration can be avoided, the adverse side effects lowered, and the compliance of the patients enhanced.

IC ICM A61K009-70

ICS A61K045-06; A61P009-12

CC 63-6 (Pharmaceuticals)

ST **patch** controlled transdermal delivery hypertension

IT Adrenoceptor agonists  
Antihypertensives

Calcium channel blockers

Diuretics

Human

(controlled release **patch** for treating hypertension)

IT Fluoropolymers, biological studies

Polyolefins

Polysiloxanes, biological studies

RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(controlled release **patch** for treating hypertension)

IT **Drug delivery systems**

(**transdermal**, controlled-release; controlled release

**patch** for treating hypertension)

IT Adrenoceptor antagonists

( $\alpha$ -; controlled release **patch** for treating hypertension)

IT Adrenoceptor antagonists

( $\beta$ -; controlled release **patch** for treating hypertension)

IT 87333-19-5, Ramipril

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(controlled release **patch** for treating hypertension)

IT 7429-90-5, Aluminum, biological studies 9002-84-0, Poly(tetrafluoroethylene) 9002-86-2, Polyvinyl chloride 9002-88-4, Polyethylene 9003-07-0, Polypropylene 9003-27-4, Polyisobutylene 9003-39-8, Polyvinylpyrrolidone 9004-35-7 9012-09-3 24937-78-8, Ethylene-vinyl acetate copolymer 106107-54-4, Butadiene-styrene block copolymer 117318-45-3, Ethylene-butadiene block copolymer  
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(controlled release **patch** for treating hypertension)

IT 58-93-5, Hydrochlorothiazide 9002-18-0, Agar 51384-51-1, Metoprolol 59227-89-3, Azone 72509-76-3, Felodipine

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(controlled release **patch** for treating hypertension)

IT 87333-19-5, Ramipril

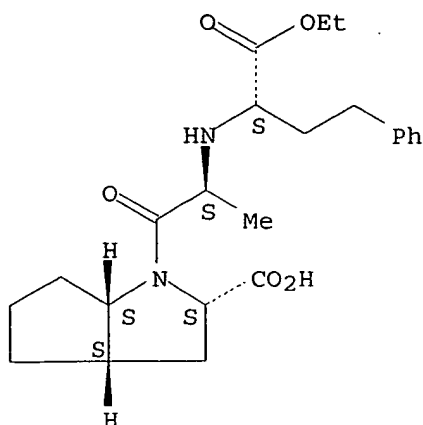
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(controlled release **patch** for treating hypertension)

RN 87333-19-5 HCAPLUS

CN Cyclopenta[b]pyrrole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,6aS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L264 ANSWER 12 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2004:902163 HCAPLUS  
 DOCUMENT NUMBER: 141:355412  
 TITLE: Transdermal delivery systems for tranquilizers and sedatives  
 INVENTOR(S): Mutzbauer, Till S.  
 PATENT ASSIGNEE(S): Switz.  
 SOURCE: PCT Int. Appl., 20 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004091589	A1	20041028	WO 2004-DE766	20040414
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				

DE 10317108	A1	20041111	DE 2003-10317108	20030414
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PRIORITY APPLN. INFO.: DE 2003-10317108 A 20030414

AB An externally administrable agent, particularly a transdermal system for treating states of agitation or for use in preoperative sedation, contains, in an **adhesive** dressing preparation, a pharmaceutically effective amount of propofol (2,6-diisopropyl phenol) or of benzodiazepine or of another consciousness-suppressing agent. **Plasters** with **adhesives**, release layers and backing foils are prepared; ointment and cream based formulations can be used.

IC ICM A61K009-70

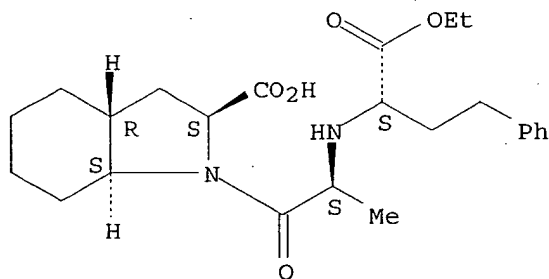
ICS A61K031-05; A61P023-00

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1

ST transdermal tranquilizer sedative **plaster** cream ointment  
 IT **Drug delivery systems**  
 (ointments, creams; **transdermal** delivery systems for  
 tranquilizers and sedatives)  
 IT **Drug delivery systems**  
 (ointments; **transdermal** delivery systems for tranquilizers  
 and sedatives)  
 IT **Adhesives**  
 Hypnotics and Sedatives  
**Permeation enhancers**  
 Tranquilizers  
 (transdermal delivery systems for tranquilizers and sedatives)  
 IT **Drug delivery systems**  
 (transdermal, **plaster**; **transdermal**  
 delivery systems for tranquilizers and sedatives)  
 IT 2078-54-8, Propofol 12794-10-4D, Benzodiazepine, derivs.  
 87679-37-6, Trandolapril  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (transdermal delivery systems for tranquilizers and sedatives)  
 IT 87679-37-6, Trandolapril  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
 (transdermal delivery systems for tranquilizers and sedatives)  
 RN 87679-37-6 HCAPLUS  
 CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-  
 phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aR,7aS)- (9CI) (CA INDEX  
 NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L264 ANSWER 13 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2004:589364 HCAPLUS  
 DOCUMENT NUMBER: 141:117196  
 TITLE: Nitrosated and nitrosylated rapamycin compounds,  
 compositions and methods of use  
 INVENTOR(S): Garvey, David S.  
 PATENT ASSIGNEE(S): Nitromed, Inc., USA  
 SOURCE: PCT Int. Appl., 89 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004060283	A2	20040722	WO 2003-US39562	20031215
WO 2004060283	A3	20050324		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003293529	A1	20040729	AU 2003-293529	20031215
US 2005209266	A1	20050922	US 2005-135308	20050524
PRIORITY APPLN. INFO.:				
			US 2002-433595P	P 20021216
			US 2003-513215P	P 20031023
			WO 2003-US39562	W 20031215

OTHER SOURCE(S): MARPAT 141:117196

AB The invention describes novel nitrosated and/or nitrosylated rapamycin compds., and novel compns. comprising at least one nitrosated and/or nitrosylated rapamycin compound, and, optionally, at least one compound that donates, transfers or releases nitric oxide, elevates endogenous levels of endothelium-derived relaxing factor, stimulates endogenous synthesis of nitric oxide or is a substrate for nitric oxide synthase and/or at least one therapeutic agent. The invention also provides novel compns. comprising at least one rapamycin compound and at least one compound that donates, transfers or releases nitric oxide, elevates endogenous levels of endothelium-derived relaxing factor, stimulates endogenous synthesis of nitric oxide or is a substrate for nitric oxide synthase and/or at least one therapeutic agent. The compds. and compns. of the invention can also be bound to a matrix. The invention also provides methods for treating and/or preventing cardiovascular diseases, for the prevention of platelet aggregation and platelet adhesion caused by the exposure of blood to a medical device, for treating and/or preventing pathol. conditions resulting from abnormal cell proliferation; transplantation rejections; autoimmune, inflammatory, proliferative, hyperproliferative or vascular diseases; for reducing scar tissue or for inhibiting wound contraction, particularly the prophylactic and/or therapeutic treatment of restenosis by administering nitrosated and/or nitrosylated rapamycin compds. or rapamycin compds. in combination with nitric oxide donors that are capable of releasing nitric oxide or indirectly delivering or transferring nitric oxide to targeted sites under physiol. conditions.

IC ICM A61K

CC 1-12 (Pharmacology)

Section cross-reference(s): 63

IT Polyamides, biological studies

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (aromatic, dendrimers, **matrix**, formulation with; nitrosated and nitrosylated rapamycin compds. for release of nitric oxide use to treat diseases in combination with other nitric oxide donors and other agents)

IT Polymers, biological studies

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (block, **matrix**, formulation with; nitrosated and nitrosylated rapamycin compds. for release of nitric oxide use to treat diseases in combination with other nitric oxide donors and other agents)

IT Polymers, biological studies

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(co-, **matrix**, formulation with; nitrosated and nitrosylated rapamycin compds. for release of nitric oxide use to treat diseases in combination with other nitric oxide donors and other agents)

IT Biopolymers  
Fibers  
Polyamides, biological studies  
Polyanhydrides  
Polyesters, biological studies  
Polyethers, biological studies  
Polymers, biological studies  
Polyolefins  
Polyurethanes, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(**matrix**, formulation with; nitrosated and nitrosylated rapamycin compds. for release of nitric oxide use to treat diseases in combination with other nitric oxide donors and other agents)

IT Dendritic polymers  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(polyamides, aromatic, **matrix**, formulation with; nitrosated and nitrosylated rapamycin compds. for release of nitric oxide use to treat diseases in combination with other nitric oxide donors and other agents)

IT Drug delivery systems  
(**transdermal**; nitrosated and nitrosylated rapamycin compds. for release of nitric oxide use to treat diseases in combination with other nitric oxide donors and other agents)

IT 9015-82-1, Angiotensin converting enzyme 9015-94-5, Renin, biological studies 82707-54-8, Neutral endopeptidase 329900-75-6, Cyclooxygenase 2 433935-36-5, Polymerase  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(**inhibitors**; nitrosated and nitrosylated rapamycin compds. for release of nitric oxide use to treat diseases in combination with other nitric oxide donors and other agents)

IT 9002-98-6, Polyethylenimine 26063-00-3, Polyhydroxybutyrate  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(**matrix**, formulation with; nitrosated and nitrosylated rapamycin compds. for release of nitric oxide use to treat diseases in combination with other nitric oxide donors and other agents)

IT 9015-82-1, Angiotensin converting enzyme  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(**inhibitors**; nitrosated and nitrosylated rapamycin compds. for release of nitric oxide use to treat diseases in combination with other nitric oxide donors and other agents)

RN 9015-82-1 HCAPLUS  
CN Carboxypeptidase, dipeptidyl, A (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

L264 ANSWER 14 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:352951 HCAPLUS

DOCUMENT NUMBER: 140:350582

TITLE: Methods and combination compositions using antioxidants, nitrosated compounds, and other agents for the treatment of vascular diseases characterized by nitric oxide insufficiency

INVENTOR(S): Loscalzo, Joseph; Vita, Joseph A.; Loberg, Michael D.; Worcel, Manuel

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 28 pp., Cont.-in-part of U.S.  
6,635,273.  
CODEN: USXXCO  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 5  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004081642	A1	20040429	US 2003-687706	20031020
US 6635273	B1	20031021	US 2000-697317	20001027
PRIORITY APPLN. INFO.:			US 1999-162230P	P 19991029
			US 2000-179020P	P 20000131
			US 2000-697317	A2 20001027

OTHER SOURCE(S): MARPAT 140:350582

AB The invention provides methods of treating or preventing vascular diseases caused by nitric oxide (NO) insufficiency. The methods encompass administering a composition comprising an antioxidant, a compound to treat cardiovascular diseases, a nitrosated compound, a compound that donates, transfers or releases NO, or is a NO synthase substrate, or endogenously stimulates NO synthesis, or stimulates levels of endothelium derived relaxing factor. In the composition, a hydralazine compound may be an antioxidant, isosorbide mono-or dinitrate may be the compound to donate, transfer, release, or stimulate endogenous NO synthesis. The isosorbide may also elevate endogenous levels of endothelium-derived relaxing factor, or be a NO synthase substrate and angiotensin enzyme inhibitor may be nitrosated compound. Disclosed in the invention is also a method to treat, or prevent Renaud's syndrome by administering a therapeutically effective amount of an antioxidant, a NO donor, a nitrosated compound and novel sustained-release formulations (e.g. a transdermal **patch**).

IC ICM A61K009-00

ICS A61K009-52

INCL 424094100; 424400000

CC 1-8 (Pharmacology)

Section cross-reference(s): 63

ST vascular disease NO insufficiency treatment antioxidant cardiovascular drug; nitrosated compd NO donor vascular disease NO insufficiency treatment; hydralazine isosorbide nitrate vascular disease NO insufficiency treatment; Renaud's syndrome treatment antioxidant nitrosated compd NO donor; sustained release pharmaceutical vascular disease NO insufficiency treatment; transdermal **patch** vascular disease NO insufficiency treatment

IT **Drug delivery systems**

(**transdermal**; antioxidants, nitrosated compds., and other agents for treatment of vascular diseases characterized by nitric oxide insufficiency)

IT 9015-82-1, **Angiotensin converting enzyme**

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(**inhibitors**, and nitrosated **ACE inhibitors**

; antioxidants, nitrosated compds., and other agents for treatment of vascular diseases characterized by nitric oxide insufficiency)

IT 9015-82-1, **Angiotensin converting enzyme**

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(**inhibitors**, and nitrosated **ACE inhibitors**

; antioxidants, nitrosated compds., and other agents for treatment of vascular diseases characterized by nitric oxide insufficiency)

RN 9015-82-1 HCAPLUS

CN Carboxypeptidase, dipeptidyl, A (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

L264 ANSWER 15 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:363685 HCAPLUS

DOCUMENT NUMBER: 140:380637

TITLE: Stabilisation of pharmaceutical compositions comprising **ACE inhibitor** by absence of acidic excipients having large specific surface area, e.g. silicon dioxide

INVENTOR(S): Bergman, Jeffrey; Mantri, Pranita S.

PATENT ASSIGNEE(S): Niche Generics Limited, UK; Unichem Laboratories Limited

SOURCE: Brit. UK Pat. Appl., 50 pp.

CODEN: BAXXDU

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2394660	A1	20040505	GB 2003-29232	20031217
PRIORITY APPLN. INFO.:			GB 2003-29232	20031217
OTHER SOURCE(S):	MARPAT 140:380637			

AB The present invention relates to stable pharmaceutical compns. comprising an ACE inhibitor (which are otherwise susceptible to degradation due to cyclisation, hydrolysis and oxidation). This is achieved by providing compns. substantially free of any acidic excipients having a large sp. surface area, especially substantially free of colloidal silicon dioxide. The composition also comprises one or more excipients, which are preferably compatible with the ACE inhibitor. The ACE inhibitor is preferably perindopril or ramipril. The composition may be used as a medicament for the treatment or prevention of a cardiovascular disorder, hypertension, coronary heart disease or a cerebrovascular disease. The composition may further comprise a  $\beta$ -blocker, a diuretic, a calcium-channel blocker, a vasodilator anti-hypertensive drug, or an angiotensin II receptor antagonist.

IC ICM A61K047-00

ICS A61K031-404; A61K038-05; A61P009-00; A61P009-12

CC 63-6 (Pharmaceuticals)

ST stable **ACE inhibitor** absence acidic excipient  
antihypertensive cardiovascular disease

IT Drug delivery systems  
(aerosols, airway; stabilization of pharmaceutical compns. comprising **ACE inhibitor** by absence of acidic excipients having large sp. surface area like silicon dioxide)

IT Angiotensin receptor antagonists  
(angiotensin II; stabilization of pharmaceutical compns. comprising **ACE inhibitor** by absence of acidic excipients having large sp. surface area like silicon dioxide)

IT Drug delivery systems  
(caplets; stabilization of pharmaceutical compns. comprising **ACE inhibitor** by absence of acidic excipients having large sp. surface area like silicon dioxide)

IT Drug delivery systems  
(capsules; stabilization of pharmaceutical compns. comprising **ACE inhibitor** by absence of acidic excipients having large sp. surface area like silicon dioxide)

- IT Brain, disease  
(cerebrovascular, treatment of; stabilization of pharmaceutical compns. comprising **ACE inhibitor** by absence of acidic excipients having large sp. surface area like silicon dioxide)
- IT Artery, disease  
(coronary, treatment of; stabilization of pharmaceutical compns. comprising **ACE inhibitor** by absence of acidic excipients having large sp. surface area like silicon dioxide)
- IT Metals, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(earth alkaline; stabilization of pharmaceutical compns. comprising **ACE inhibitor** by absence of acidic excipients having large sp. surface area like silicon dioxide)
- IT Drug delivery systems  
(granules; stabilization of pharmaceutical compns. comprising **ACE inhibitor** by absence of acidic excipients having large sp. surface area like silicon dioxide)
- IT Drug delivery systems  
(lozenges; stabilization of pharmaceutical compns. comprising **ACE inhibitor** by absence of acidic excipients having large sp. surface area like silicon dioxide)
- IT Drug delivery systems  
(oral; stabilization of pharmaceutical compns. comprising **ACE inhibitor** by absence of acidic excipients having large sp. surface area like silicon dioxide)
- IT Drug delivery systems  
(parenterals; stabilization of pharmaceutical compns. comprising **ACE inhibitor** by absence of acidic excipients having large sp. surface area like silicon dioxide)
- IT Drug delivery systems  
(powders; stabilization of pharmaceutical compns. comprising **ACE inhibitor** by absence of acidic excipients having large sp. surface area like silicon dioxide)
- IT Drug delivery systems  
(rectal; stabilization of pharmaceutical compns. comprising **ACE inhibitor** by absence of acidic excipients having large sp. surface area like silicon dioxide)
- IT Carboxylic acids, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(saturated C16-24; stabilization of pharmaceutical compns. comprising **ACE inhibitor** by absence of acidic excipients having large sp. surface area like silicon dioxide)
- IT Antihypertensives  
Binders  
Calcium channel blockers  
Cardiovascular system, disease  
Diuretics  
Lubricants  
Vasodilators  
(stabilization of pharmaceutical compns. comprising **ACE inhibitor** by absence of acidic excipients having large sp. surface area like silicon dioxide)
- IT Alkali metal hydroxides  
Carbohydrates, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(stabilization of pharmaceutical compns. comprising **ACE inhibitor** by absence of acidic excipients having large sp. surface area like silicon dioxide)
- IT Zea mays  
(starch; stabilization of pharmaceutical compns. comprising **ACE**

- inhibitor** by absence of acidic excipients having large sp. surface area like silicon dioxide)
- IT Drug delivery systems  
(tablet disintegrant; stabilization of pharmaceutical compns. comprising **ACE inhibitor** by absence of acidic excipients having large sp. surface area like silicon dioxide)
- IT Drug delivery systems  
(tablets; stabilization of pharmaceutical compns. comprising **ACE inhibitor** by absence of acidic excipients having large sp. surface area like silicon dioxide)
- IT Drug delivery systems  
(topical; stabilization of pharmaceutical compns. comprising **ACE inhibitor** by absence of acidic excipients having large sp. surface area like silicon dioxide)
- IT Drug delivery systems  
(transdermal; stabilization of pharmaceutical compns. comprising **ACE inhibitor** by absence of acidic excipients having large sp. surface area like silicon dioxide)
- IT Hypertension  
(treatment of; stabilization of pharmaceutical compns. comprising **ACE inhibitor** by absence of acidic excipients having large sp. surface area like silicon dioxide)
- IT Drug delivery systems  
(vaginal; stabilization of pharmaceutical compns. comprising **ACE inhibitor** by absence of acidic excipients having large sp. surface area like silicon dioxide)
- IT Adrenoceptor antagonists  
( $\beta$ -; stabilization of pharmaceutical compns. comprising **ACE inhibitor** by absence of acidic excipients having large sp. surface area like silicon dioxide)
- IT 7631-86-9, Colloidal silicon dioxide, uses  
RL: NUU (Other use, unclassified); USES (Uses)  
(colloidal; stabilization of pharmaceutical compns. comprising **ACE inhibitor** by absence of acidic excipients having large sp. surface area like silicon dioxide)
- IT 9015-82-1  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(**inhibitors**; stabilization of pharmaceutical compns. comprising **ACE inhibitor** by absence of acidic excipients having large sp. surface area like silicon dioxide)
- IT 9005-25-8, Starch, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(maize, pregelatinised; stabilization of pharmaceutical compns. comprising **ACE inhibitor** by absence of acidic excipients having large sp. surface area like silicon dioxide)
- IT 9004-34-6, Cellulose, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(microcryst.; stabilization of pharmaceutical compns. comprising **ACE inhibitor** by absence of acidic excipients having large sp. surface area like silicon dioxide)
- IT 63-42-3, Lactose 69-65-8, Mannitol 557-04-0, Magnesium stearate 4070-80-8, Sodium stearyl fumarate 7757-93-9, Dibasic calcium phosphate 9003-39-8, Polyvinylpyrrolidone 9063-38-1, Sodium starch glycolate 14265-44-2, Phosphate, biological studies 14807-96-6, Talc, biological studies 30388-04-6, Stenopril 62571-86-2, Captopril 74258-86-9, Alacepril 75847-73-3, Enalapril 76420-72-9, Enalaprilat 76547-98-3, Lisinopril 80830-42-8, Rentiapril 81872-10-8, Zofenopril 82834-16-0, Perindopril 82924-03-6, Pentopril 83435-66-9, Delapril 83647-97-6, Spirapril 85441-61-8, Quinapril 85856-54-8, Moveltipril 86541-75-5, Benazepril 87333-19-5,

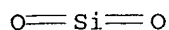
Ramipril 87679-37-6, TrandOlapril 88768-40-5,  
 Cilazapril 89371-37-9, Imidapril 98048-97-6,  
 Fosinopril 99880-64-5, Glycerol dibehenate 103775-10-6,  
 Moexipril 107133-36-8, Perindopril erbumine 109214-55-3,  
 Libenzapril 111223-26-8, Ceronapril 111902-57-9, Temocapril

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (stabilization of pharmaceutical compns. comprising **ACE**  
**inhibitor** by absence of acidic excipients having large sp.  
 surface area like silicon dioxide)

IT 7631-86-9, Colloidal silicon dioxide, uses  
 RL: NUU (Other use, unclassified); USES (Uses)  
 (colloidal; stabilization of pharmaceutical compns. comprising  
**ACE inhibitor** by absence of acidic excipients having  
 large sp. surface area like silicon dioxide)

RN 7631-86-9 HCAPLUS

CN Silica (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



IT 9015-82-1

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (inhibitors; stabilization of pharmaceutical compns.  
 comprising **ACE inhibitor** by absence of acidic  
 excipients having large sp. surface area like silicon dioxide)

RN 9015-82-1 HCAPLUS

CN Carboxypeptidase, dipeptidyl, A (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

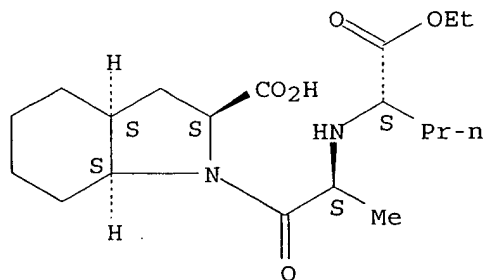
IT 82834-16-0, Perindopril 83647-97-6, Spirapril  
 86541-75-5, Benazepril 87333-19-5, Ramipril  
 87679-37-6, TrandOlapril 88768-40-5, Cilazapril  
 89371-37-9, Imidapril 98048-97-6, Fosinopril  
 103775-10-6, Moexipril 107133-36-8, Perindopril erbumine

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (stabilization of pharmaceutical compns. comprising **ACE**  
**inhibitor** by absence of acidic excipients having large sp.  
 surface area like silicon dioxide)

RN 82834-16-0 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(  
 (ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)- (9CI)  
 (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

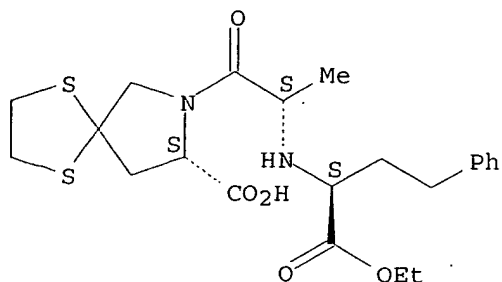


RN 83647-97-6 HCAPLUS

CN 1,4-Dithia-7-azaspiro[4.4]nonane-8-carboxylic acid, 7-[(2S)-2-[[[(1S)-1-

(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-, (8S)- (9CI) (CA INDEX NAME)

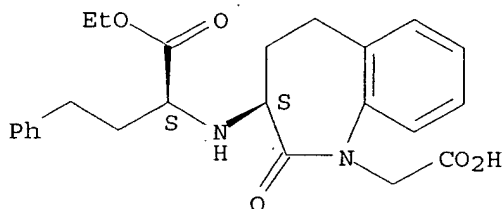
Absolute stereochemistry. Rotation (-).



RN 86541-75-5 HCAPLUS

CN 1H-1-Benzazepine-1-acetic acid, 3-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-2,3,4,5-tetrahydro-2-oxo-, (3S)- (9CI) (CA INDEX NAME)

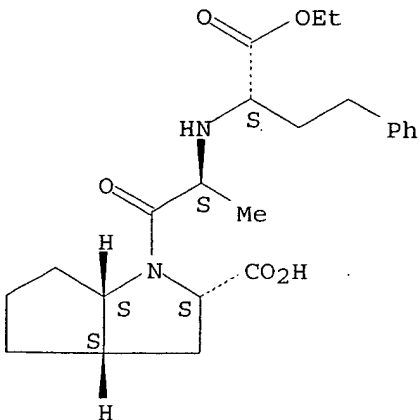
Absolute stereochemistry.



RN 87333-19-5 HCAPLUS

CN Cyclopenta[b]pyrrole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,6aS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

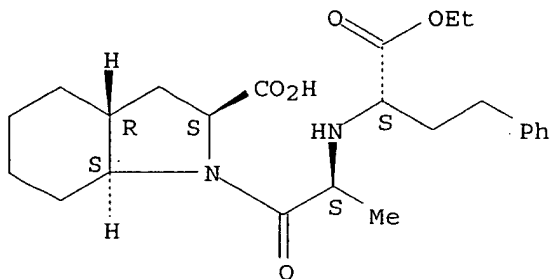


RN 87679-37-6 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-

phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aR,7aS)- (9CI) (CA INDEX NAME)

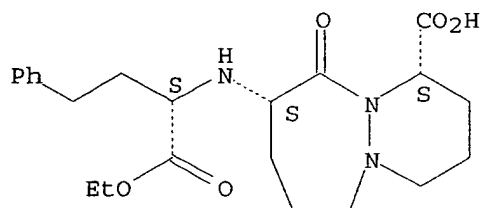
Absolute stereochemistry. Rotation (-).



RN 88768-40-5 HCAPLUS

CN 6H-Pyridazino[1,2-a][1,2]diazepine-1-carboxylic acid, 9-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]octahydro-10-oxo-, (1S,9S)- (9CI) (CA INDEX NAME)

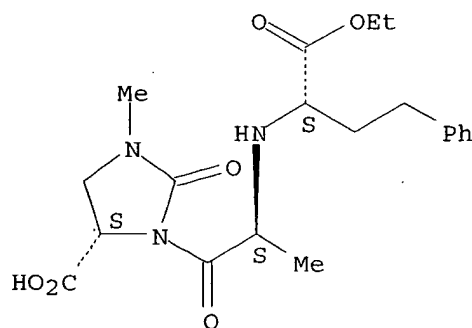
Absolute stereochemistry.



RN 89371-37-9 HCAPLUS

CN 4-Imidazolidinecarboxylic acid, 3-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1-methyl-2-oxo-, (4S)- (9CI) (CA INDEX NAME)

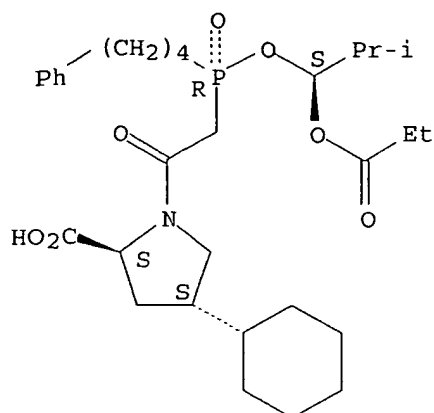
Absolute stereochemistry.



RN 98048-97-6 HCAPLUS

CN L-Proline, 4-cyclohexyl-1-[[[(R)-[(1S)-2-methyl-1-(1-oxopropoxy)propoxy] (4-phenylbutyl)phosphinyl]acetyl]-, (4S)- (9CI) (CA INDEX NAME)

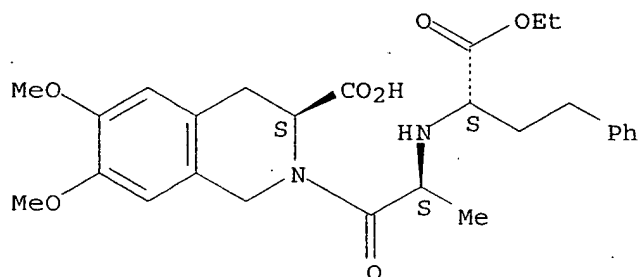
Absolute stereochemistry.



RN 103775-10-6 HCAPLUS

CN 3-Isoquinolinecarboxylic acid, 2-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-6,7-dimethoxy-, (3S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 107133-36-8 HCAPLUS

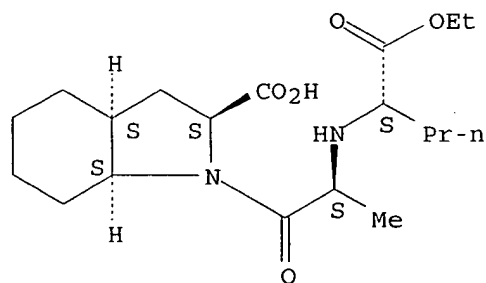
CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)butyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,7aS)-, compd. with 2-methyl-2-propanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 82834-16-0

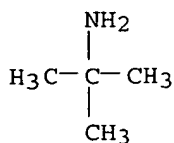
CMF C19 H32 N2 O5

Absolute stereochemistry. Rotation (-).



CM 2

CRN 75-64-9  
CMF C4 H11 N



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L264 ANSWER 16 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:836762 HCAPLUS

DOCUMENT NUMBER: 139:350474

TITLE: Preparation and compositions of nitrosothio  
(hetero)cyclic nitric oxide donors

INVENTOR(S): Fang, Xinqin; Garvey, David S.; Gaston, Ricky D.; Lin, Chia-en; Ranatunga, Ramani R.; Richardson, Stewart K.; Wang, Tiansheng; Wang, Weiheng; Wey, Shio-jyi

PATENT ASSIGNEE(S): Nitromed, Inc., USA

SOURCE: PCT Int. Appl., 138 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

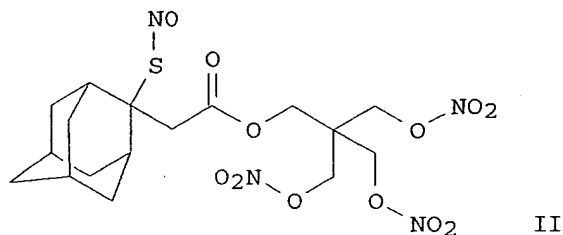
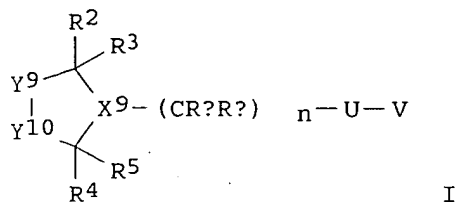
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003086282	A2	20031023	WO 2003-US10562	20030407
WO 2003086282	A3	20040429		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
CA 2480832	AA	20031023	CA 2003-2480832	20030407
AU 2003223491	A1	20031027	AU 2003-223491	20030407
US 2003203915	A1	20031030	US 2003-407420	20030407
EP 1497268	A2	20050119	EP 2003-719621	20030407
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
JP 2005537223	T2	20051208	JP 2003-583309	20030407
PRIORITY APPLN. INFO.:			US 2002-369873P	P 20020405
			WO 2003-US10562	W 20030407

OTHER SOURCE(S): MARPAT 139:350474

GI



AB Title compds. I [wherein U = O, S, or NRaRi; V = NO or NO<sub>2</sub>; X<sub>9</sub> = CR<sub>10</sub> or N; Y<sub>9</sub> = CR<sub>6</sub>R<sub>7</sub>, NR<sub>i</sub>, NR<sub>25</sub>, NR<sub>i</sub>CR<sub>6</sub>R<sub>7</sub>, CR<sub>6</sub>R<sub>7</sub>NR<sub>i</sub>, CR<sub>2</sub>R<sub>3</sub>CR<sub>6</sub>R<sub>7</sub>, or CR<sub>6</sub>R<sub>7</sub>CR<sub>2</sub>R<sub>3</sub>; Y<sub>10</sub> = CR<sub>8</sub>R<sub>9</sub> or CR<sub>8</sub>R<sub>9</sub>CR<sub>17</sub>R<sub>18</sub>; R<sub>2</sub>-R<sub>9</sub>, R<sub>17</sub>, and R<sub>18</sub> = independently H or alkyl; or R<sub>2</sub>R<sub>3</sub>, R<sub>4</sub>R<sub>5</sub>, R<sub>6</sub>R<sub>7</sub>, or R<sub>8</sub>R<sub>9</sub> = independently oxo; or R<sub>4</sub> and R<sub>7</sub> together with the C's to which they are attached = cycloalkyl; or CR<sub>6</sub>R<sub>7</sub> = cycloalkyl; R<sub>6</sub> and R<sub>9</sub> taken together with the C's to which they are attached = (bridged)cycloalkyl, heterocyclyl, or aryl with the proviso that R<sub>7</sub> and R<sub>8</sub> are not present; R<sub>4</sub> and R<sub>25</sub> taken together with the C and N to which they are attached = heterocyclyl; R<sub>a</sub> = lone pair of electrons, H, or (aryl)alkyl; R<sub>e</sub> and R<sub>f</sub> = independently H, halo, OH, or (un)substituted (cyclo)alkyl, heterocyclyl, alkoxy, amino, aryl, etc.; or CR<sub>e</sub>R<sub>f</sub> = heterocyclyl or (bridged) cycloalkyl; R<sub>i</sub> = H or (un)substituted alkyl, aryl, carboxamido, sulfonamido, etc.; n = 0-3; and pharmaceutically acceptable salts thereof] were prepared as novel nitric oxide donors for use in compns. comprising at least one nitric oxide donor and optionally at least one therapeutic agent. The nitric oxide donors donate, transfer or release nitric oxide, and/or elevate endogenous levels of endothelium-derived relaxing factor, and/or stimulate endogenous synthesis of nitric oxide and/or are substrates for nitric oxide synthase and are capable of releasing nitric oxide or indirectly delivering or transferring nitric oxide to targeted sites under physiol. conditions (no data). For example, 2-[2-(nitrosothio)adamantan-2-yl]acetic acid was esterified with 3-nitrooxy-2,2-bis(nitrooxymethyl)propan-1-ol in the presence of 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide•HCl and 4-dimethylaminopyridine in CH<sub>2</sub>Cl<sub>2</sub> to give II (18%). The latter inhibited proliferation of human coronary artery smooth muscle cells with IC<sub>50</sub> of 5 μM. In general, the nitrosylated compds. tested in this assay inhibited proliferation of vascular smooth muscle cells, while the corresponding non-nitrosylated derivs. showed no inhibition, slight inhibition, or exhibited much higher IC<sub>50</sub> values. Thus, the invention provides methods for treating cardiovascular diseases, for the inhibition of platelet aggregation and platelet adhesion caused by the exposure of blood to a medical device, for treating pathol. conditions resulting from abnormal cell proliferation, transplantation rejections, autoimmune, inflammatory, proliferative, hyperproliferative, vascular diseases, for reducing scar tissue or for inhibiting wound contraction, particularly the

prophylactic and/or therapeutic treatment of restenosis (no data). The invention also provides methods for treating inflammation, pain, fever, gastrointestinal disorders, respiratory disorders, and sexual dysfunctions (no data). In addition, the invention provides novel compns. and kits comprising at least one nitric oxide donor and/or at least one therapeutic agent.

IC ICM A61K

CC 24-1 (Alicyclic Compounds)

Section cross-reference(s): 1, 27, 28, 63

IT **Medical goods**

(bags, dialysis, composition delivery; preparation and compns. of nitrosothio

(hetero)cyclic nitric oxide donors for treatment of cardiovascular, proliferative, inflammatory, and autoimmune disorders and other conditions)

IT **Medical goods**

(balloon, composition delivery; preparation and compns. of nitrosothio (hetero)cyclic nitric oxide donors for treatment of cardiovascular, proliferative, inflammatory, and autoimmune disorders and other conditions)

IT **Medical goods**

(bandages, composition delivery; preparation and compns. of nitrosothio (hetero)cyclic nitric oxide donors for treatment of cardiovascular, proliferative, inflammatory, and autoimmune disorders and other conditions)

IT **Medical goods**

(catheters, composition delivery; preparation and compns. of nitrosothio (hetero)cyclic nitric oxide donors for treatment of cardiovascular, proliferative, inflammatory, and autoimmune disorders and other conditions)

IT **Medical goods**

(complications associated with use; preparation and compns. of nitrosothio (hetero)cyclic nitric oxide donors for treatment of cardiovascular, proliferative, inflammatory, and autoimmune disorders and other conditions)

IT **Medical goods**

(stents, composition delivery; preparation and compns. of nitrosothio (hetero)cyclic nitric oxide donors for treatment of cardiovascular, proliferative, inflammatory, and autoimmune disorders and other conditions)

IT **Medical goods**

(sutures, composition delivery; preparation and compns. of nitrosothio (hetero)cyclic nitric oxide donors for treatment of cardiovascular, proliferative, inflammatory, and autoimmune disorders and other conditions)

IT **Drug delivery systems**

(transdermal; preparation and compns. of nitrosothio (hetero)cyclic nitric oxide donors for treatment of cardiovascular, proliferative, inflammatory, and autoimmune disorders and other conditions)

IT **Medical goods**

(wires, composition delivery; preparation and compns. of nitrosothio (hetero)cyclic nitric oxide donors for treatment of cardiovascular, proliferative, inflammatory, and autoimmune disorders and other conditions)

IT 9015-82-1

RL: BSU (Biological study, unclassified); BIOL (Biological study) (inhibitors, composition component; preparation and compns. of nitrosothio (hetero)cyclic nitric oxide donors for treatment of cardiovascular, proliferative, inflammatory, and autoimmune disorders

and other conditions)

IT 9015-82-1

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(**inhibitors**, composition component; preparation and compns. of  
nitrosothio (hetero)cyclic nitric oxide donors for treatment of  
cardiovascular, proliferative, inflammatory, and autoimmune disorders  
and other conditions)

RN 9015-82-1 HCAPLUS

CN Carboxypeptidase, dipeptidyl, A (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

L264 ANSWER 17 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:492692 HCAPLUS

DOCUMENT NUMBER: 139:57966

TITLE: Preparation of pharmaceuticals containing carbohydrate  
moieties

INVENTOR(S): Christian, Samuel T.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 32 pp., Cont.-in-part of U.S.  
Ser. No. 547,506.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003119761	A1	20030626	US 2002-198798	20020718
US 6548484	B1	20030415	US 2000-547506	20000412
US 2005250739	A1	20051110	US 2003-625645	20030722
PRIORITY APPLN. INFO.:			US 2000-547506	A2 20000412
			US 2000-547501	A2 20000412
			US 2002-198798	B2 20020718

OTHER SOURCE(S): MARPAT 139:57966

AB Hydrophilic N-linked pharmaceutical compns., methods of their preparation and  
use in drug delivery comprise a glycosyl CNS acting prodrug compound  
covalently N-linked with a saccharide through an amide or an amine bond  
and a formulary consisting of an additive, a stabilizer, a carrier, a  
binder, a buffer, an excipient, an emollient, a disintegrant, a  
lubricating agent, an antimicrobial agent or a preservative, with the  
proviso that the saccharide moiety is not a cyclodextrin or a glucuronide.  
Gluconolactone and 3-hydroxytryamine were reacted slowly in methanol to  
form a white solid dopamine gluconamide precipitant. The product was  
collected by filtration, washing and drying in vacuo. Tablets for oral  
administration were prepared from the dopamine gluconamide 250, starch 17,  
sodium starch glycolate 40, PVP 7.0, microcryst. cellulose 45, and Mg  
stearate 2.0 mg.

IC ICM A61K031-7052

ICS A61K009-14; A61K009-70

INCL 514042000; 424449000; 424489000

CC 63-6 (Pharmaceuticals)

IT **Medical goods**

(**bandages**; preparation of pharmaceuticals containing carbohydrate  
moieties)

IT **Drug delivery systems**

(**transdermal**; preparation of pharmaceuticals containing carbohydrate  
moieties)

IT 9015-82-1, ACE

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibitor; preparation of pharmaceuticals containing carbohydrate  
moieties)

IT 9015-82-1, ACE

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibitor; preparation of pharmaceuticals containing carbohydrate  
moieties)

RN 9015-82-1 HCAPLUS

CN Carboxypeptidase, dipeptidyl, A (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

L264 ANSWER 18 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:521509 HCAPLUS

DOCUMENT NUMBER: 137:88482

TITLE: Combined use of enzyme inhibitors and pharmaceutical  
preparations thereof for the treatment and prophylaxis  
of arteriosclerosis, type I allergic reactions, and  
dermatological diseases associated with follicular and  
epidermal hyperkeratosis

INVENTOR(S): Ansorge, Siegfried; Lendeckel, Uwe; Neubert, Klaus;  
Reinhold, Dirk; Vetter, Robert; Gollnick, Harald

PATENT ASSIGNEE(S): Institut Fuer Medizintechnologie Magdeburg G.m.b.H.,  
Germany

SOURCE: PCT Int. Appl., 40 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002053170	A2	20020711	WO 2001-EP15199	20011221
WO 2002053170	A3	20030220		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
DE 10100052	A1	20020711	DE 2001-10100052	20010102
DE 10102392	A1	20020814	DE 2001-10102392	20010119
DE 10155093	A1	20030612	DE 2001-10155093	20011109
CA 2436724	AA	20020711	CA 2001-2436724	20011221
EP 1349576	A2	20031008	EP 2001-984881	20011221
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
JP 2004520330	T2	20040708	JP 2002-554119	20011221
US 2004132639	A1	20040708	US 2004-250476	20040212
PRIORITY APPLN. INFO.:			DE 2001-10100052	A 20010102
			DE 2001-10102392	A 20010119
			DE 2001-10155093	A 20011109
			WO 2001-EP15199	W 20011221

OTHER SOURCE(S): MARPAT 137:88482

AB The invention discloses the use of inhibitors of dipeptidyl peptidase IV  
(DPP IV) and enzymes having the same substrate specificity, combined with

inhibitors of alanyl aminopeptidase (aminopeptidase N), or enzymes having the same substrate specificity, for the additive to superadditive inhibition of the activation and proliferation (DNA synthesis) of human T lymphocytes or mononuclear cells and of the production of TH2 cytokines for the treatment and prevention of allergic reactions of type I (according to the Gell and Coombs classification), for the additive to superadditive inhibition of the activation and proliferation (DNA synthesis) of human epidermal and follicular keratinocytes and those of the transition region between the skin and the mucosa, and for the treatment and prevention of dermatol. diseases associated with follicular and epidermal hyperkeratosis and increased keratinocyte proliferation. The invention also discloses the use of DPP IV and enzymes having the same substrate specificity, combined with inhibitors of aminopeptidase N or enzymes having the same substrate specificity, inhibitors of X-pro-aminopeptidase (aminopeptidase P), inhibitors of angiotensin-converting enzyme (ACE) and/or of prolyl oligopeptidase (prolyl endopeptidase) for the additive to superadditive inhibition of the activation, DNA synthesis and proliferation of human T lymphocytes or mononuclear cells for the treatment and prophylaxis of arteriosclerosis. The invention further discloses pharmaceutical prepsns. comprising a plurality of inhibitors of the above enzymes.

- IC ICM A61K038-00  
 CC 1-12 (Pharmacology)  
 Section cross-reference(s): 63  
 ST enzyme inhibitor arteriosclerosis allergy dermatol disease; dipeptidyl peptidase IV inhibitor arteriosclerosis allergy dermatol disease;  
**angiotensin converting enzyme inhibitor** arteriosclerosis allergy dermatol disease; alanyl aminopeptidase inhibitor arteriosclerosis allergy dermatol disease; aminopeptidase P inhibitor arteriosclerosis allergy dermatol disease; prolyl oligopeptidase inhibitor arteriosclerosis allergy dermatol disease; prolyl endopeptidase inhibitor arteriosclerosis allergy dermatol disease  
 IT **Medical goods**  
 (bandages, hydrocolloid; enzyme inhibitor combinations for treatment of arteriosclerosis, type I allergic reactions, and dermatol. diseases associated with follicular and epidermal hyperkeratosis)  
 IT **Drug delivery systems**  
 (transdermal; enzyme inhibitor combinations for treatment of arteriosclerosis, type I allergic reactions, and dermatol. diseases associated with follicular and epidermal hyperkeratosis)  
 IT **9015-82-1, Angiotensin-converting enzyme** 9054-63-1, Alanyl aminopeptidase 37288-66-7, Aminopeptidase P 54249-88-6, Dipeptidyl peptidase IV 72162-84-6, Prolyl endopeptidase  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (enzyme **inhibitor** combinations for treatment of arteriosclerosis, type I allergic reactions, and dermatol. diseases associated with follicular and epidermal hyperkeratosis)  
 IT 2817-45-0, Phosphoramidic acid 2817-45-0D, Phosphoramidic acid, derivs. 13434-13-4, Actinonin 17721-06-1, 3-Thiophenamine 41721-00-0 41721-00-0D, derivs. 54164-07-7 54164-07-7D, derivs. 56384-04-4D, N $\alpha$ -protected 58970-76-6, Bestatin 62023-67-0 62571-86-2, Captopril 65921-40-6 65921-40-6D, derivs. 67655-94-1, Amastatin 75847-73-3, Enalapril 76547-98-3, Lisinopril **88768-40-5**, Cilazapril 99429-59-1 123652-87-9, Probestin 129085-76-3, Leuhistin 136259-18-2 136259-18-2D, derivs. 136259-19-3 136259-19-3D, derivs. 136259-20-6 136259-20-6D, derivs. 136259-21-7 136259-21-7D, derivs. 136259-22-8 136259-22-8D, derivs. 136259-23-9D, N $\alpha$ -protected 137563-63-4, Eurystatin A 137563-64-5, Eurystatin B 142880-55-5 142880-55-5D, derivs. 148152-02-7 148152-02-7D, derivs. 160470-73-5,

Apstatin 184360-42-7 187402-73-9, Phebestin 192821-27-5  
192821-27-5D, derivs. 202599-70-0 251571-76-3 251571-76-3D, derivs.  
252860-55-2 252860-55-2D, derivs. 252860-56-3 252860-57-4  
252860-58-5 327983-79-9 327983-79-9D, derivs. 376346-22-4  
376346-22-4D, derivs. 376346-23-5D, N $\alpha$ -protected 376346-25-7D,  
N $\alpha$ -protected 441022-63-5 441022-67-9 441022-69-1 441022-70-4  
441022-77-1 441022-79-3

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(enzyme inhibitor combinations for treatment of arteriosclerosis, type  
I allergic reactions, and dermatol. diseases associated with follicular  
and epidermal hyperkeratosis)

IT 9015-82-1, Angiotensin-converting  
enzyme

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(enzyme inhibitor combinations for treatment of  
arteriosclerosis, type I allergic reactions, and dermatol. diseases  
associated with follicular and epidermal hyperkeratosis)

RN 9015-82-1 HCAPLUS

CN Carboxypeptidase, dipeptidyl, A (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

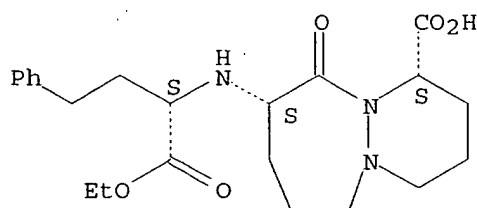
IT 88768-40-5, Cilazapril

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(enzyme inhibitor combinations for treatment of arteriosclerosis, type  
I allergic reactions, and dermatol. diseases associated with follicular  
and epidermal hyperkeratosis)

RN 88768-40-5 HCAPLUS

CN 6H-Pyridazino[1,2-a][1,2]diazepine-1-carboxylic acid, 9-[[[(1S)-1-  
(ethoxycarbonyl)-3-phenylpropyl]amino]octahydro-10-oxo-, (1S,9S)- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.



L264 ANSWER 19 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:332068 HCAPLUS

DOCUMENT NUMBER: 136:335235

TITLE: Methods of treating vascular diseases characterized by  
nitric oxide insufficiency

INVENTOR(S): Loscalzo, Joseph; Vita, Joseph A.; Loberg, Michael D.;  
Worcel, Manuel

PATENT ASSIGNEE(S): Nitromed, Inc., USA; Trustees of Boston University

SOURCE: PCT Int. Appl., 64 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002034303	A1	20020502	WO 2001-US14245	20010502
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
WO 2001035961	A1	20010525	WO 2000-US29528	20001027
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6635273	B1	20031021	US 2000-697317	20001027
CA 2421885	AA	20020502	CA 2001-2421885	20010502
AU 2001059399	A5	20020506	AU 2001-59399	20010502
EP 1337283	A1	20030827	EP 2001-932915	20010502
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004521083	T2	20040715	JP 2002-537354	20010502
PRIORITY APPLN. INFO.:				
			US 2000-697317	A 20001027
			WO 2000-US29528	W 20001027
			US 1999-162230P	P 19991029
			US 2000-179020P	P 20000131
			WO 2001-US14245	W 20010502

OTHER SOURCE(S): MARPAT 136:335235

AB The present invention provides methods of treating or preventing vascular diseases caused by nitric oxide (NO) insufficiency. The methods encompass administering a composition comprising an antioxidant, a compound to treat cardiovascular diseases, a nitrosated compound, a compound that donates, transfers or releases NO, or is a NO synthase substrate, or endogenously stimulates NO synthesis, or stimulates levels of endothelium derived relaxing factor. In the said composition, a hydralazine compound may be an antioxidant, isosorbide mono-or dinitrate may be the compound to donate, transfer, release, or stimulate endogenous NO synthesis. The isosorbide may also elevate endogenous levels of endothelium-derived relaxing factor, or be a NO synthase substrate and angiotensin enzyme inhibitor may be nitrosated compound. Disclosed in the invention is also a method to treat, or prevent Reynaud's syndrome by administering a therapeutically effective amount of an antioxidant, a NO donor, a nitrosated compound and novel sustained-release formulations (e.g. a transdermal patch).

IC ICM A61L015-16

CC 1-7 (Pharmacology)

Section cross-reference(s): 14, 63

IT Drug delivery systems

(sustained-release, patches; methods of treating vascular diseases characterized by nitric oxide insufficiency)

IT Drug delivery systems

(transdermal, sustained-release; methods of treating vascular diseases characterized by nitric oxide insufficiency)

IT 9015-82-1 9015-94-5, Renin, biological studies

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(**inhibitors**, nitrosated; methods of treating vascular  
diseases characterized by nitric oxide insufficiency)

IT 9015-82-1

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(**inhibitors**, nitrosated; methods of treating vascular  
diseases characterized by nitric oxide insufficiency)

RN 9015-82-1 HCAPLUS

CN Carboxypeptidase, dipeptidyl, A (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L264 ANSWER 20 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:964930 HCAPLUS

DOCUMENT NUMBER: 138:29171

TITLE: Transdermal and topical administration of  
antihypertensive agents using basic enhancers

INVENTOR(S): Luo, Eric C.; Jacobson, Eric C.; Hsu, Tsung-Min

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 15 pp., Cont.-in-part of U.S.  
Ser. No. 972,008.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 26

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002192301	A1	20021219	US 2002-175682	20020619
US 2001051166	A1	20011213	US 2000-738410	20001214
US 6586000	B2	20030701		
US 2002018803	A1	20020214	US 2000-738395	20001214
US 6719997	B2	20040413		
US 2002034554	A1	20020321	US 2001-972008	20011004
US 6582724	B2	20030624		
ZA 2002004671	A	20030611	ZA 2002-4671	20020611
US 2005074487	A1	20050407	US 2004-863432	20040607
PRIORITY APPLN. INFO.:			US 1999-465098	A2 19991216
			US 2000-569889	A2 20000511
			US 2000-607892	B2 20000630
			US 2000-738395	A2 20001214
			US 2000-738410	A2 20001214
			US 2001-972008	A2 20011004
			US 2002-175681	A2 20020619
			US 2002-175682	A2 20020619
			US 2002-175721	B2 20020619
			US 2002-175769	B2 20020619
			US 2002-176264	A2 20020619
			US 2002-176265	A3 20020619
			US 2002-176952	B2 20020621
			US 2003-675603	A2 20030929

AB Methods are provided for enhancing the permeability of skin or mucosal  
tissue to topical or transdermal application of antihypertensive agents.  
The methods entail the use of a base in order to increase the flux of the  
agent through a body surface while minimizing the likelihood of skin  
damage, irritation or sensitization. The permeation enhancer can be an  
inorg. or organic base. Compns. and transdermal systems are also described.

For example, the cumulative amount of enalapril maleate across human cadaver skin at 24 h from transdermal patch increased from 0.029 mg/cm<sup>2</sup> to 1.826 mg/cm<sup>2</sup> when the calculated excess NaOH concentration in the dried patch was increased from 1.9% to 6.9%, as compared to undetectable flux for formulation without NaOH.

IC ICM A61K033-02  
ICS A61K033-00  
INCL 424719000; 424722000  
CC 63-6 (Pharmaceuticals)  
Section cross-reference(s): 1  
IT Drug delivery systems  
(topical; transdermal and topical administration of antihypertensive agents using basic enhancers)  
IT Drug delivery systems  
(transdermal; transdermal and topical administration of antihypertensive agents using basic enhancers)  
IT 9015-82-1, Angiotensin converting enzyme  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibitors; transdermal and topical administration of antihypertensive agents using basic enhancers)  
IT 9015-82-1, Angiotensin converting enzyme  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibitors; transdermal and topical administration of antihypertensive agents using basic enhancers)  
RN 9015-82-1 HCAPLUS  
CN Carboxypeptidase, dipeptidyl, A (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

L264 ANSWER 21 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:868260 HCAPLUS

DOCUMENT NUMBER: 136:627

TITLE: Combinations of enzyme inhibitor-containing preparations and the use in inhibition of mononuclear cells and T-cells and treatment of immune conditions

INVENTOR(S): Ansorge, Siegfried; Arndt, Marco; Buehling, Frank;

PATENT ASSIGNEE(S): Lendeckel, Uwe; Neubert, Klaus; Reinhold, Dirk  
Institut fuer Medizintechnologie Magdeburg G.m.b.H.  
IMTM, Germany

SOURCE: PCT Int. Appl., 24 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001089569	A1	20011129	WO 2001-EP5887	20010522
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

DE 10025464	A1	20011206	DE 2000-10025464	20000523
CA 2410305	AA	20021122	CA 2001-2410305	20010522
EP 1289559	A1	20030312	EP 2001-945184	20010522
EP 1289559	B1	20050727		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

JP 2003534293	T2	20031118	JP 2001-585811	20010522
AU 2001267475	B2	20041104	AU 2001-267475	20010522
AT 300313	E	20050815	AT 2001-945184	20010522
ES 2243516	T3	20051201	ES 2001-1945184	20010522
US 2005014699	A1	20050120	US 2004-296102	20040326

PRIORITY APPLN. INFO.:

DE 2000-10025464	A	20000523
WO 2001-EP5887	W	20010522

AB A method is disclosed which permits, owing to the simultaneous and joint inhibition of the enzyme activities of (1) alanyl-aminopeptidase and dipeptidyl-peptidase IV, (2) dipeptidyl-peptidase IV and angiotensin-converting enzyme, (3) dipeptidyl-peptidase IV and prolyl-oligopeptidase, and (4) dipeptidyl-peptidase IV and X-Pro-aminopeptidase, the inhibition of DNA synthesis and thus the proliferation of mononuclear cells and T cells to an extent which cannot be obtained by individual application of the enzyme inhibitors, even when used in higher doses. Although the above-mentioned inhibitors influence the same process, namely DNA synthesis and thus the proliferation of immune cells, this effect is not complete and not long-lasting when the inhibitors are used individually. The functional overlapping of enzymic activities results, as is supported by exptl. data, in an additive/superadditive inhibitory effect on DNA synthesis and the proliferation resulting from the simultaneous inhibition of a plurality of the above enzymes. The invention shows that the simultaneous application of inhibitors of the above enzymes or of corresponding preps. and forms of administration is suitable for the therapy of autoimmune diseases and chronic diseases with an inflammatory genesis, as well as for the treatment of post-transplant rejection episodes.

ICM A61K045-06

ICS A61P037-06; A61P035-00; A61K038-55; A61K038-55

CC 1-7 (Pharmacology)

ST peptidase **ACE inhibitor** combination immune disorder;  
mononuclear cell antiproliferative peptidase **ACE inhibitor** combination; T cell antiproliferative peptidase **ACE inhibitor** combination; autoimmune disease peptidase **ACE inhibitor** combination; transplant rejection peptidase **ACE inhibitor** combination

IT **Medical goods**

(bandages, hydrocolloid; enzyme inhibitor combinations for inhibition of mononuclear cells and T-cells and treatment of immune conditions)

IT **Drug delivery systems**

(transdermal; enzyme inhibitor combinations for inhibition of mononuclear cells and T-cells and treatment of immune conditions)

IT 9015-82-1, Angiotensin-converting

enzyme 9054-63-1, Alanyl amino-peptidase 37288-66-7, Amino-peptidase P 54249-88-6, Dipeptidyl-peptidase IV 72162-84-6, Prolyl oligopeptidase

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(enzyme **inhibitor** combinations for **inhibition** of mononuclear cells and T-cells and treatment of immune conditions)

IT 72-18-4D, L-Valine, amidated 73-22-3D, L-Tryptophan, amidated  
73-32-5D, L-Isoleucine, amidated 147-85-3D, L-Proline, amidated  
2577-48-2 3557-90-2D, amidated 13434-13-4, Actinonin 41721-00-0  
54164-07-7 56384-04-4 62023-67-0 62571-86-2, Captopril 65921-40-6

75847-73-3, Enalapril 76547-98-3, Lisinopril **88768-40-5**,  
 Cilazapril 88795-32-8 99429-59-1 123652-87-9, Probestin  
 129085-76-3, Leuhistin 135219-43-1, Poststatin 136259-18-2  
 136259-19-3 136259-20-6 136259-21-7 136259-22-8 136259-23-9  
 137563-63-4, Eurystatin A 137563-64-5, Eurystatin B 142880-55-5  
 148152-02-7 160470-73-5, Apstatin 184360-42-7 187402-73-9, Phebestin  
 192821-27-5 251571-76-3 252860-55-2 252860-56-3 252860-57-4  
 252860-58-5 327623-45-0 327983-79-9 376346-22-4 376346-23-5  
 376346-24-6 376346-25-7 376346-26-8 376346-27-9

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);  
 THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (enzyme inhibitor combinations for inhibition of mononuclear cells and  
 T-cells and treatment of immune conditions)

IT **9015-82-1, Angiotensin-converting  
 enzyme**

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (enzyme **inhibitor** combinations for **inhibition** of  
 mononuclear cells and T-cells and treatment of immune conditions)

RN 9015-82-1 HCAPLUS

CN Carboxypeptidase, dipeptidyl, A (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

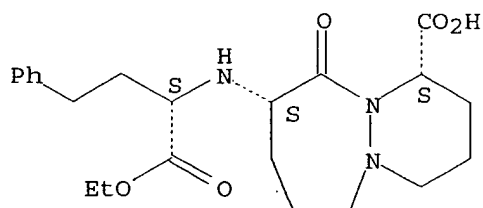
IT **88768-40-5, Cilazapril**

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);  
 THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (enzyme inhibitor combinations for inhibition of mononuclear cells and  
 T-cells and treatment of immune conditions)

RN 88768-40-5 HCAPLUS

CN 6H-Pyridazino[1,2-a][1,2]diazepine-1-carboxylic acid, 9-[[[(1S)-1-  
 (ethoxycarbonyl)-3-phenylpropyl]amino]octahydro-10-oxo-, (1S,9S)- (9CI)  
 (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L264 ANSWER 22 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:380401 HCAPLUS

DOCUMENT NUMBER: 135:9996

TITLE: Methods of treating vascular diseases characterized by  
 nitric oxide insufficiency

INVENTOR(S): Loscalzo, Joseph; Vita, Joseph A.; Loberg, Michael D.;  
 Worcel, Manuel

PATENT ASSIGNEE(S): Nitromed, Inc., USA; Trustees of Boston University

SOURCE: PCT Int. Appl., 44 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5

## PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001035961	A1	20010525	WO 2000-US29528	20001027
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2386954	AA	20010525	CA 2000-2386954	20001027
AU 2001014393	A5	20010530	AU 2001-14393	20001027
AU 780261	B2	20050310		
EP 1244455	A1	20021002	EP 2000-976651	20001027
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003514020	T2	20030415	JP 2001-537954	20001027
CA 2421885	AA	20020502	CA 2001-2421885	20010502
WO 2002034303	A1	20020502	WO 2001-US14245	20010502
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001059399	A5	20020506	AU 2001-59399	20010502
EP 1337283	A1	20030827	EP 2001-932915	20010502
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004521083	T2	20040715	JP 2002-537354	20010502
US 2004005306	A1	20040108	US 2003-415136	20030425
PRIORITY APPLN. INFO.:			US 1999-162230P	P 19991029
			US 2000-179020P	P 20000131
			US 2000-697317	A 20001027
			WO 2000-US29528	W 20001027
			WO 2001-US14245	W 20010502
AB The present invention provides methods of treating and/or preventing vascular diseases, such as Raynaud's syndrome, where NO insufficiency is a contributing factor, by administering a therapeutically effective amount of an antioxidant, or a pharmaceutically acceptable salt thereof, and isosorbide dinitrate or isosorbide mononitrate, and, optionally, nitrosated angiotensin-converting enzyme (ACE) inhibitor, nitrosated $\beta$ -adrenergic blocker, nitrosated calcium channel blocker, nitrosated endothelin antagonist, nitrosated angiotensin II receptor antagonist, nitrosated renin inhibitor, and/or at least one compound used to treat cardiovascular diseases. The antioxidant is preferably a hydralazine compound or a pharmaceutically acceptable salt thereof. The vascular disease characterized by NO insufficiency is low-renin hypertension, salt-sensitive hypertension, low-renin salt-sensitive hypertension, primary pulmonary hypertension, thromboembolic pulmonary hypertension, pregnancy-induced hypertension, renovascular hypertension, heart failure, microvascular cardiac ischemia, and left ventricular hypertrophy with disproportionate microvascularization or diastolic dysfunction. The present invention also provides novel transdermal patches or				

oral dosage forms, such as tablets and capsules, comprising an antioxidant, isosorbide dinitrate or isosorbide mononitrate, and/or at least one nitrosated ACE inhibitor, nitrosated  $\beta$ -adrenergic blocker, nitrosated calcium channel blocker, nitrosated endothelin antagonist, nitrosated angiotensin II receptor antagonist, or nitrosated renin inhibitor.

IC ICM A61K031-535  
ICS A61K031-50; A61K031-495; A61K031-415; A61K031-355; A61K031-34; A61K031-19; A61K031-135; A01N045-00  
CC 63-6 (Pharmaceuticals)  
Section cross-reference(s): 1  
IT **Drug delivery systems**  
(transdermal, sustained-release; compns. containing antioxidants, isosorbide nitrates, and nitrosated cardiovascular agents for treating vascular diseases associated with NO insufficiency)  
IT **Drug delivery systems**  
(transdermal; compns. containing antioxidants, isosorbide nitrates, and nitrosated cardiovascular agents for treating vascular diseases associated with NO insufficiency)  
IT **9015-82-1, Angiotensin-converting enzyme** 9015-94-5, Renin, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study).  
(inhibitors, nitrosated; antioxidants, isosorbide nitrates, and nitrosated cardiovascular agents for treating vascular diseases associated with NO insufficiency)  
IT **9015-82-1, Angiotensin-converting enzyme**  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibitors, nitrosated; antioxidants, isosorbide nitrates, and nitrosated cardiovascular agents for treating vascular diseases associated with NO insufficiency)  
RN 9015-82-1 HCAPLUS  
CN Carboxypeptidase, dipeptidyl, A (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L264 ANSWER 23 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:824085 HCAPLUS

DOCUMENT NUMBER: 134:9357

TITLE: Method of treating angina and/or anginal equivalents using phospholipid liposomes

INVENTOR(S): Goldberg, Dennis I.; Williams, Kevin Jon

PATENT ASSIGNEE(S): Talaria Therapeutics, Inc., USA

SOURCE: PCT Int. Appl., 142 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000069412	A1	20001123	WO 2000-US12962	20000512
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW			

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,  
 DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,  
 CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  
 CA 2373681 AA 20001123 CA 2000-2373681 20000512  
 EP 1183011 A1 20020306 EP 2000-932314 20000512  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO  
 JP 2003508349 T2 20030304 JP 2000-617871 20000512  
 AU 773385 B2 20040527 AU 2000-50053 20000512  
 AU 2004203419 A2 20040819 AU 2004-203419 20040727  
 AU 2004203419 A1 20040819

PRIORITY APPLN. INFO.: US 1999-134140P P 19990514  
 WO 2000-US12962 W 20000512

AB The present invention provides a method of treating angina, e.g., stable angina, unstable angina and variant angina, and/or an anginal equivalent comprising administering a therapeutically effective amount of a multiplicity of liposomes, and preferably, large liposomes comprised of phospholipids substantially free of sterol to a subject for a treatment period. The method also includes administering an effective amount of an antianginal drug other than the liposomes. The invention also provides a method of treating claudication comprising administering a therapeutically effective amount of liposomes. In yet another variant, the invention provides a method of perioperative and/or pre-operative conditioning of a subject comprising administering liposomes. Several other inventions are also described herein. An antianginal drug is selected from the group consisting of a nitrate, a beta blocker, a calcium channel antagonist, a coronary vasodilator, a lipid lowering drug, an afterload reducing agent, an inotropic agent, a pre-load reducing agent, and an opiate.

IC ICM A61K009-127

ICS A61K009-133

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1

IT Polymers, biological studies

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (matrixes; phospholipid liposomes for treatment of angina  
 and/or anginal equivalent)

IT Drug delivery systems

(transdermal; phospholipid liposomes for treatment of angina  
 and/or anginal equivalent)

IT 9015-82-1

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (inhibitors; phospholipid liposomes for treatment of angina  
 and/or anginal equivalent)

IT 50-54-4, Quinidex 51-06-9, Procainamide 52-53-9, Verapamil 55-63-0,  
 Nitroglycerin 56-54-2, Quinidine 58-61-7, Adenosine, biological  
 studies 87-33-2, Isosorbide dinitrate 152-11-4, Calan 525-66-6,  
 Propranolol 3737-09-5, Disopyramide 3930-20-9, Sotalol 5370-01-4,  
 Mexilit 7697-37-2D, Nitric acid, organic esters, biological studies  
 13523-86-9, Pindolol 16051-77-7, Isosorbide 5-mononitrate 19774-82-4,  
 Cordarone 20830-75-5, Digoxin 21829-25-4, Nifedipine 26839-75-8,  
 Timolol 27790-75-6D, Dihydropyridine, derivs. 29560-58-5, Ethmozine  
 34183-22-7, Rythmol 37517-30-9, Acebutolol 38363-40-5, Penbutolol  
 42200-33-9, Nadolol 42399-41-7, Diltiazem 51781-06-7, Carteolol  
 54143-56-5, Tambacor 55985-32-5, Nicardipine 62571-86-2, Captopril  
 64706-54-3, Bepridil 72509-76-3, Felodipine 75695-93-1, Isradipine  
 75847-73-3, Enalapril 76095-16-4, Vasotec 76420-72-9, Enalaprilat  
 76547-98-3, Zestril 81147-92-4, Esmolol 82586-52-5, Univasc  
 82586-55-8, Accupril 85441-61-8, Quinapril 86541-74-4,  
 Lotensin 86541-75-5, Benazepril 87333-19-5, Altace  
 87679-37-6, Trandolapril 88150-42-9, Amlodipine

88889-14-9, Monopril 98048-97-6, Fosinopril  
103775-10-6, Moexipril 122647-32-9, Corvert

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(phospholipid liposomes for treatment of angina and/or anginal equivalent)

IT 9015-82-1

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibitors; phospholipid liposomes for treatment of angina  
and/or anginal equivalent)

RN 9015-82-1 HCAPLUS

CN Carboxypeptidase, dipeptidyl, A (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

IT 82586-52-5, Univasc 86541-74-4, Lotensin

86541-75-5, Benazepril 87333-19-5, Altace

87679-37-6, Trandolapril 88889-14-9, Monopril

98048-97-6, Fosinopril 103775-10-6, Moexipril

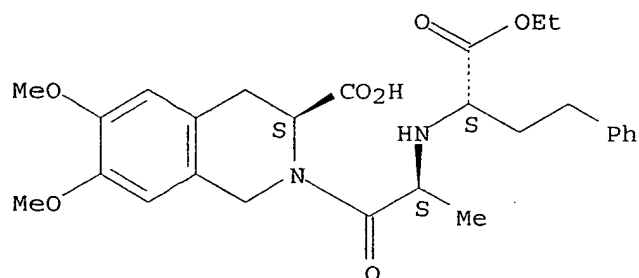
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(phospholipid liposomes for treatment of angina and/or anginal equivalent)

RN 82586-52-5 HCAPLUS

CN 3-Isoquinolinecarboxylic acid, 2-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-6,7-dimethoxy-, monohydrochloride, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

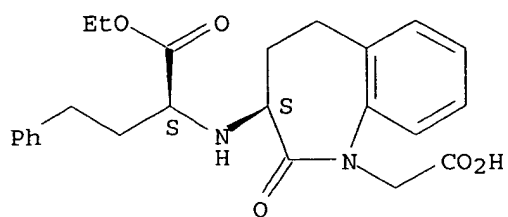


● HCl

RN 86541-74-4 HCAPLUS

CN 1H-1-Benzazepine-1-acetic acid, 3-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-2,3,4,5-tetrahydro-2-oxo-, monohydrochloride, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

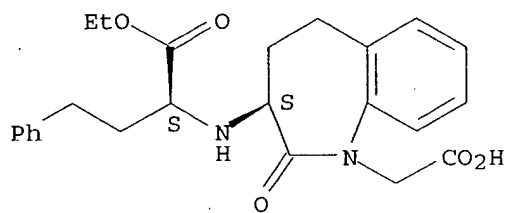


● HCl

RN 86541-75-5 HCAPLUS

CN 1H-1-Benzazepine-1-acetic acid, 3-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-2,3,4,5-tetrahydro-2-oxo-, (3S)- (9CI) (CA INDEX NAME)

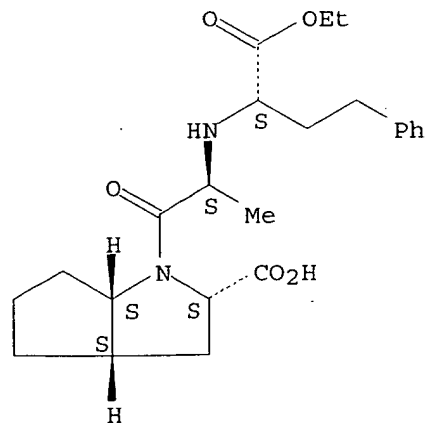
Absolute stereochemistry.



RN 87333-19-5 HCAPLUS

CN Cyclopenta[b]pyrrole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aS,6aS)- (9CI) (CA INDEX NAME)

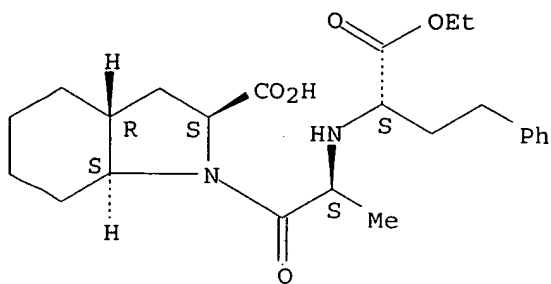
Absolute stereochemistry.



RN 87679-37-6 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 1-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]octahydro-, (2S,3aR,7aS)- (9CI) (CA INDEX NAME)

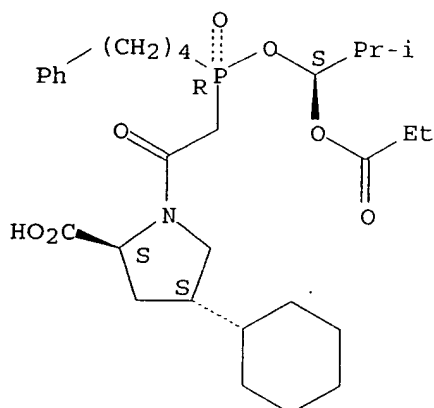
Absolute stereochemistry. Rotation (-).



RN 88889-14-9 HCAPLUS

CN L-Proline, 4-cyclohexyl-1-[[ (R)-[(1S)-2-methyl-1-(1-oxopropoxy)propoxy] (4-phenylbutyl)phosphinyl]acetyl]-, sodium salt, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

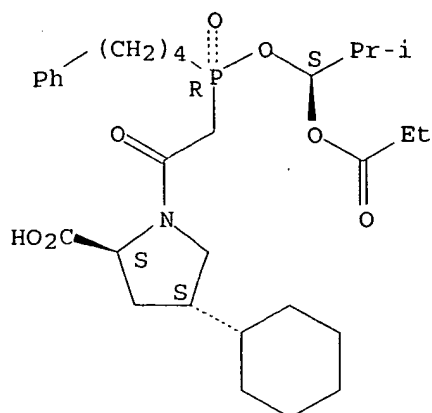


● Na

RN 98048-97-6 HCAPLUS

CN L-Proline, 4-cyclohexyl-1-[[ (R)-[(1S)-2-methyl-1-(1-oxopropoxy)propoxy] (4-phenylbutyl)phosphinyl]acetyl]-, (4S)- (9CI) (CA INDEX NAME)

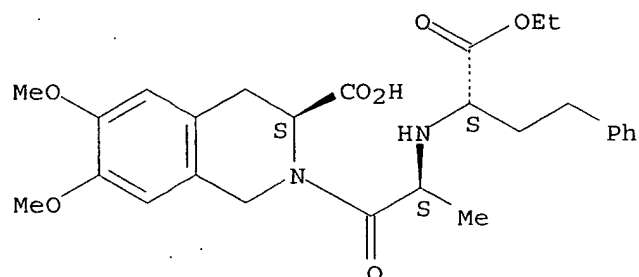
Absolute stereochemistry.



RN 103775-10-6 HCAPLUS

CN 3-Isoquinolinecarboxylic acid, 2-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1,2,3,4-tetrahydro-6,7-dimethoxy-, (3S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L264 ANSWER 24 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:553397 HCAPLUS

DOCUMENT NUMBER: 133:168375

TITLE: Method of manufacture for transdermal **matrixes**

INVENTOR(S): Audett, Jay D.; Detroyer, Georges D.

PATENT ASSIGNEE(S): Ortho-McNeil Pharmaceutical, Inc., USA

SOURCE: PCT Int. Appl., 38 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000045797	A1	20000810	WO 2000-US2491	20000201
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,				

UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,  
 DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,  
 CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

US 1999-241662

A 19990202

AB Disclosed is a method of manufacture for the production of transdermal drug delivery matrixes and devices, transdermal sampling devices, and dermal conditioning devices. A polymer and an active agent are mixed and heated in a multiple-lobed compounder to produce a polymer mixture. The polymer mixture is extruded and then at least a portion of the extrudate is formed into, for example, the transdermal drug delivery matrix, or incorporated into the transdermal drug delivery device. These alternative methods for preparing transdermal matrixes have several advantages over the current methods of manufacture. The matrix components, particularly the active agent, are not exposed to extremes in solvent or temperature for extended periods of time during the manufacture process. The transdermal matrixes prepared by these

methods perform better in transdermal devices and show greater flux of active agent. As a result of the improved performance, less active agent may be utilized during the manufacturing process, and smaller or thinner transdermal matrixes may be produced for incorporation into the corresponding transdermal device. An olanzapine transdermal matrix was prepared using a twin screw extruder as follows; HMW polyisobutylene (Vistanex L80) was blended with LMW polyisobutylene, silica gel powder, and PVP. Sep., olanzapine and lauryl lactate were processed and blended with the polymeric mixts. The resulting mixture was extruded through a sheet die and coated between a release liner and backing material. A second layer of the same extrudate was coated between a second release liner and a polyester nonwoven porous supporting layer. The release liner from the first coating pass was removed and the exposed extrudate was laminated to the nonwoven side of the second coating pass, sandwiching the porous supporting layer between the two extrudates. The rolls of laminate were converted to transdermal devices of the desired size.

IC ICM A61K009-70

CC 63-6 (Pharmaceuticals)

ST transdermal **matrix** pressure sensitive adhesive

IT Alcohols, biological studies

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (aliphatic, C12-18; manufacture of transdermal **matrixes** using  
 pressure-sensitive adhesives)

IT Deodorants (personal)

(breath fresheners; manufacture of transdermal **matrixes** using  
 pressure-sensitive adhesives)

IT Ion channel blockers

(calcium; manufacture of transdermal **matrixes** using  
 pressure-sensitive adhesives)

IT Pruritus

(inhibitors; manufacture of transdermal **matrixes** using  
 pressure-sensitive adhesives)

IT Adrenoceptor agonists

Adrenoceptor antagonists

Allergy inhibitors

Analgesics

Anesthetics

Anthelmintics

Anti-inflammatory agents

Antianginal agents

Antiarrhythmics

Antiarthritics

Antiasthmatics

Antibiotics  
 Anticoagulants  
 Anticonvulsants  
 Antidepressants  
 Antidiabetic agents  
 Antidiarrheals  
 Antiemetics  
 Antihistamines  
 Antihypertensives  
 Antimalarials  
 Antimigraine agents  
 Antioxidants  
 Antiparkinsonian agents  
 Antipsychotics  
 Antipyretics  
 Antirheumatic agents  
 Antitumor agents  
 Antitussives  
 Antiviral agents  
 Anxiolytics  
 Appetite depressants  
 Cardiotonics  
 Cholinergic agonists  
 Cholinergic antagonists  
 Contraceptives  
 Decongestants  
 Diuretics  
 Fungicides  
 Hypnotics and Sedatives  
 Immunostimulants  
 Immunosuppressants  
 Muscle relaxants  
 Psychostimulants  
 Tranquilizers  
 Vaccines  
 Vasodilators

(manufacture of transdermal **matrixes** using pressure-sensitive adhesives)

- IT Estrogens  
 Growth promoters, animal  
 Hormones, animal, biological studies  
 Isobutylene rubber  
 Progestogens  
 Steroids, biological studies  
 Vitamins  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (manufacture of transdermal **matrixes** using pressure-sensitive adhesives)
- IT Chronotropics  
 (neg.; manufacture of transdermal **matrixes** using pressure-sensitive adhesives)
- IT Essential oils  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (peppermint; manufacture of transdermal **matrixes** using pressure-sensitive adhesives)
- IT Adhesives  
 (pressure-sensitive; manufacture of transdermal **matrixes** using pressure-sensitive adhesives)
- IT Muscle relaxants  
 (spasmolytics; manufacture of transdermal **matrixes** using

pressure-sensitive adhesives)

IT Essential oils  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(spearmint; manufacture of transdermal **matrixes** using pressure-sensitive adhesives)

IT Drug delivery systems  
(transdermal; manufacture of transdermal **matrixes** using pressure-sensitive adhesives)

IT Essential oils  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(wintergreen; manufacture of transdermal **matrixes** using pressure-sensitive adhesives)

IT 9015-82-1  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(**inhibitors**; manufacture of transdermal **matrixes** using pressure-sensitive adhesives)

IT 9003-27-4  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(isobutylene rubber, manufacture of transdermal **matrixes** using pressure-sensitive adhesives)

IT 50-28-2, 17 $\beta$ -Estradiol, biological studies 51-98-9, Norethindrone acetate 52-28-8, Codeine phosphate 53-16-7, Estrone, biological studies 57-63-6, Ethinyl estradiol 57-83-0, Progesterone, biological studies 57-91-0, 17 $\alpha$ -Estradiol 58-22-0, Testosterone 68-22-4, Norethindrone 72-33-3, Mestranol 89-78-1, Menthol 94-09-7, Benzocaine 94-14-4, Isobutamben 94-24-6, Tetracaine 111-46-6, Diethylene glycol, biological studies 125-69-9, Dextromethorphan hydrobromide 128-62-1, Noscapine 137-58-6, Lidocaine 152-43-2, Quinestrol 434-22-0, 19-Nortestosterone 474-86-2, Equilin 547-64-8, Methyl lactate 586-60-7, Dyclonine 797-63-7, Levonorgestrel 1155-03-9, Zolamine hydrochloride 1622-61-3, Clonazepam 6283-92-7, Lauryl lactate 6533-00-2, Norgestrel 9003-27-4, Polyisobutylene 9003-39-8, Kollidon 9004-64-2, Hydroxypropyl cellulose 27194-74-7, Propylene glycol monolaurate 35189-28-7, Norgestimate 53016-31-2, 17-Deacetylnorgestimate 54024-22-5, Desogestrel 72509-76-3, Felodipine 106133-20-4, Tamsulosin 132539-06-1, Olanzapine  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(manufacture of transdermal **matrixes** using pressure-sensitive adhesives)

IT 9015-82-1  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(**inhibitors**; manufacture of transdermal **matrixes** using pressure-sensitive adhesives)

RN 9015-82-1 HCAPLUS

CN Carboxypeptidase, dipeptidyl, A (9CI). (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L264 ANSWER 25 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:636276 HCAPLUS

DOCUMENT NUMBER: 133:198702

TITLE: S-acetylcaptopril preparation as angiotensin  
-converting enzyme  
inhibitor

INVENTOR(S): Xie, Meihua

PATENT ASSIGNEE(S): Shanghai Inst. of Pharmaceutical Industry, State  
Pharmaceutical Administration, Peop. Rep. China

SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 10 pp.

DOCUMENT TYPE: CODEN: CNXXEV  
 LANGUAGE: Patent  
 FAMILY ACC. NUM. COUNT: 1 Chinese  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1232667	A	19991027	CN 1998-110794	19980421
PRIORITY APPLN. INFO.:			CN 1998-110794	19980421

AB S-acetylcaptopril injection is composed of S-acetylcaptopril 0.01-50, NaCl 0.45-2.7, benzyl alc. 1-3, buffer solution 0.01-10, and water for injection 10-99%. S-acetylcaptopril hard capsule is composed of S-acetylcaptopril 0.1-50, starch or modified starch 5-90, microcryst. cellulose or powdered cellulose 0-50, lactose 0-80, CaSO<sub>4</sub> 0-40, CaHPO<sub>4</sub> 0-20, cellulose derivative 0-20, stearic acid or its salt 0.3-1, talc 0-6, silica gel superfine powder 0-3, and water 0-10%. S-acetylcaptopril soft capsule is composed of S-acetylcaptopril 0.1-50, mannitol 0-30, polyethylene glycol 1-60, glycerol 0.1-30, polyvinylpyrrolidone 0-20, sorbitol 0-30, surfactants 0-5, silica gel superfine powder 0-3, water 0-50, ethanol 0-50, and coloring matter 0-5%. S-acetylcaptopril membrane is composed of S-acetylcaptopril 0.1-50, polyvinyl alc. 1-98, acrylic resin high mol. material 0-98, glycerol 0.1-10, TiO<sub>2</sub> or silica gel superfine powder 0-3, ethanol 0-20, and water 0-20%. The fast release part in S-acetylcaptopril sustained-release preparation is composed of S-acetylcaptopril 0.1-30, lactose 0-60, starch or modified starch 5-40, microcryst. cellulose or powdered cellulose 0-50, cellulose derivative 0-20, CMC 0-30, PVP 0-20, Mg stearate 0.3-1, talc 0-6, ethanol 0-10, and water 1-10%. The sustained-release part in S-acetylcaptopril sustained-release preparation is composed of S-acetylcaptopril 0.1-30, dextrin 0-20, starch or modified starch 0-50, acacia or other natural gel 0-20, cellulose derivative 0-60, acrylic resin 0-50, sucrose 0-20, microcryst. cellulose or powdered cellulose 0-50, lakh or other natural gel 0-20, stearic acid or its salt 0-3, talc 0-6, water 1-10, and ethanol 0-10%. An ointment for S-acetylcaptopril transdermal drug release preparation is composed of S-acetylcaptopril 0.1-30, glyceryl monostearate 1-30, stearic acid 1-40, vaseline 1-30, K-12 0.1-10, glycerol 1-20, water. The compns. for paste and suppository are presented. The compns. may contain hydragogue dihydrochlorothiazide or Ca antagonist amlodipine mesylate.

IC ICM A61K031-40  
 ICS A61K009-00

CC 63-6 (Pharmaceuticals)  
 Section cross-reference(s): 1

IT Cardiovascular agents  
 (S-acetylcaptopril preparation as **angiotensin-converting enzyme inhibitor**)

IT Drug delivery systems  
 (capsules; S-acetylcaptopril preparation as **angiotensin-converting enzyme inhibitor**)

IT Drug delivery systems  
 (injections; S-acetylcaptopril preparation as **angiotensin-converting enzyme inhibitor**)

IT Drug delivery systems  
 (suppositories; S-acetylcaptopril preparation as **angiotensin-converting enzyme inhibitor**)

IT Drug delivery systems  
 (sustained-release; S-acetylcaptopril preparation as **angiotensin-converting enzyme inhibitor**)

IT Drug delivery systems  
 (tablets; S-acetylcaptopril preparation as **angiotensin-**

converting enzyme inhibitor)

IT Drug delivery systems  
(transdermal; S-acetylcaptopril preparation as angiotensin  
-converting enzyme inhibitor)

IT 56-81-5, Glycerol, biological studies 57-11-4, Stearic acid, biological  
studies 58-93-5, Dihydrochlorothiazide 63-42-3, Lactose 69-65-8,  
Mannitol 557-04-0, Magnesium stearate 7631-86-9, Silica,  
biological studies 7757-93-9, Calcium hydrogen phosphate 7778-18-9,  
Calcium sulfate 9002-89-5, Polyvinyl alcohol 9003-39-8,  
Polyvinylpyrrolidone 64838-55-7, S-Acetylcaptopril 111470-99-6,  
Amlodipine besylate  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(S-acetylcaptopril preparation as angiotensin-converting  
enzyme inhibitor)

IT 9015-82-1, Angiotensin-converting  
enzyme  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(inhibitor; S-acetylcaptopril preparation as angiotensin  
-converting enzyme inhibitor)

IT 7631-86-9, Silica, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(S-acetylcaptopril preparation as angiotensin-converting  
enzyme inhibitor)

RN 7631-86-9 HCAPLUS  
CN Silica (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

O=Si=O

IT 9015-82-1, Angiotensin-converting  
enzyme  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(inhibitor; S-acetylcaptopril preparation as angiotensin  
-converting enzyme inhibitor)

RN 9015-82-1 HCAPLUS  
CN Carboxypeptidase, dipeptidyl, A (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

L264 ANSWER 26 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 1996:137854 HCAPLUS  
DOCUMENT NUMBER: 124:185605  
TITLE: Transdermal pharmaceutical compositions of  
antihypertensives for controlling the initial release  
time  
INVENTOR(S): Takagi, Yasuyoshi; Goto, Yoshito; Sato, Makoto  
PATENT ASSIGNEE(S): Sanwa Kagaku Kenkyusho Co, Japan  
SOURCE: Jpn. Kokai Tokkyo Koho, 8 pp.  
CODEN: JKXXAF  
DOCUMENT TYPE: Patent  
LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 07330627	A2	19951219	JP 1994-120152	19940601
PRIORITY APPLN. INFO.:			JP 1994-120152	19940601
AB Transdermal pharmaceutical compns. of antihypertensives for controlling				

the initial release time are prepared by mixing active ingredients ( calcium antagonists: i.e. angiotensin I-converting enzyme inhibitors such as nicardipine hydrochloride) with hydrophilic substances (C1-4 alcs. and/or C2-40 polyols), lipophilic substances (C10-20 unsatd. fatty acids and/or C10-20 aliphatic alcs.) and water-absorbing substances to give a suspension, and soaking a nonwoven fabric piece in the suspension to produce a transdermal preparation for controlling the initial release time.

IC ICM A61K045-00  
ICS A61K009-107; A61K009-70; A61K031-00  
CC 63-6 (Pharmaceuticals)  
Section cross-reference(s): 1  
IT **Pharmaceutical dosage forms**  
(transdermal, initial release time-controlled;  
transdermal pharmaceutical compns. of antihypertensives for  
controlling the initial release time)  
IT Fatty acids, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(unsatd., C10-20; transdermal pharmaceutical compns. of  
antihypertensives for controlling the initial release time)  
IT 9015-82-1, Angiotensin I-converting enzyme  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(inhibitors; transdermal pharmaceutical compns. of  
antihypertensives for controlling the initial release time)  
IT 9015-82-1, Angiotensin I-converting enzyme  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(inhibitors; transdermal pharmaceutical compns. of  
antihypertensives for controlling the initial release time)  
RN 9015-82-1 HCAPLUS  
CN Carboxypeptidase, dipeptidyl, A (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

L264 ANSWER 27 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1994:200442 HCAPLUS

DOCUMENT NUMBER: 120:200442

TITLE: Base for transdermal pharmaceuticals

comprising fatty acid esters and alcohols

INVENTOR(S): Kobayashi, Masao; Suzuki, Takehiko; Sugaya, Kayo;  
Harada, Mitsunori

PATENT ASSIGNEE(S): Tanabe Seiyaku Co., Ltd., Japan

SOURCE: Eur. Pat. Appl., 25 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 581587	A2	19940202	EP 1993-305970	19930728
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CA 2101496	AA	19940201	CA 1993-2101496	19930728
JP 06321771	A2	19941122	JP 1993-186564	19930729
PRIORITY APPLN. INFO.:			JP 1992-204587	A 19920731
			JP 1993-55245	A 19930316

AB A base for transdermal administration of pharmaceuticals, which are difficult to be absorbed transdermally, comprises a fatty acid ester and an alc. Into 100mL of a base containing iso-Pr myristate 17.9, EtOH 71.4, and water 10.7%, was dissolved 1mg of vitamin D3 (I). A patch containing above composition was administered transdermally to rats and plasma concentration of I was

measured at 24, and 48 hs after administration. The plasma concentration of I was 9.8 and 10.1 ng/mL resp., while the amount of I for control patches containing 1mg I in 100mL EtOH was less than detection limit.

- IC ICM A61K009-06  
ICS A61M035-00
- CC 63-6 (Pharmaceuticals)
- ST **base** transdermal alc fatty acid **ester**; isopropyl myristate ethanol transdermal **base**
- IT Fatty acids, **esters**  
RL: BIOL (Biological study)  
(C10-22, **esters**, **base** for transdermal pharmaceuticals containing alcs. and)
- IT Fatty acids, **esters**  
RL: BIOL (Biological study)  
(C12-18, **esters**, **base** for transdermal pharmaceuticals containing alcs. and)
- IT Alcohols, biological studies  
Glycols, biological studies  
RL: BIOL (Biological study)  
(**base** for transdermal pharmaceuticals containing fatty acid **esters** and)
- IT Alcohols, biological studies  
RL: BIOL (Biological study)  
(C1-30, **base** for transdermal pharmaceuticals containing fatty acid **esters** and)
- IT Alcohols, biological studies  
RL: BIOL (Biological study)  
(C2-12, **base** for transdermal pharmaceuticals containing fatty acid **esters** and)
- IT Fatty acids, **esters**  
RL: BIOL (Biological study)  
(**esters**, **base** for transdermal pharmaceuticals containing alcs. and)
- IT Alcohols, biological studies  
RL: BIOL (Biological study)  
(polyhydric, **base** for transdermal pharmaceuticals containing fatty acid **esters** and)
- IT **Pharmaceutical dosage forms**  
(transdermal, **base** for, containing fatty acid **esters** and alcs.)
- IT Alcohols, biological studies  
RL: BIOL (Biological study)  
(trihydric, **base** for transdermal pharmaceuticals containing fatty acid **esters** and)
- IT 56-81-5D, 1,2,3-Propanetriol, **esters** with fatty acids  
110-27-0, Isopropyl myristate 123-95-5, Butyl stearate 142-91-6,  
Isopropyl palmitate 2311-46-8, Isopropyl capronate 2311-59-3,  
Isopropyl caprate 25496-72-4, Glyceryl monooleate 25618-55-7D,  
Polyglycerin, **esters** with fatty acids 36675-34-0D,  
Hexaglycerin, **esters** with fatty acids 51555-31-8D,  
Pentaglycerin, **esters** with fatty acids 52006-45-8, Isocetyl  
isostearate 56090-54-1D, Triglycerin, **esters** with fatty acids  
56491-53-3D, Tetraglycerin, **esters** with fatty acids  
59113-36-9D, Diglycerin, **esters** with fatty acids 83826-43-1,  
Octyldodecyl myristate  
RL: BIOL (Biological study)  
(**base** for transdermal pharmaceuticals containing alcs. and)
- IT 64-17-5, Ethanol, biological studies 67-63-0, Isopropyl alcohol,  
biological studies 112-92-5, Stearyl alcohol  
RL: BIOL (Biological study)

(base for transdermal pharmaceuticals containing fatty acid esters and)

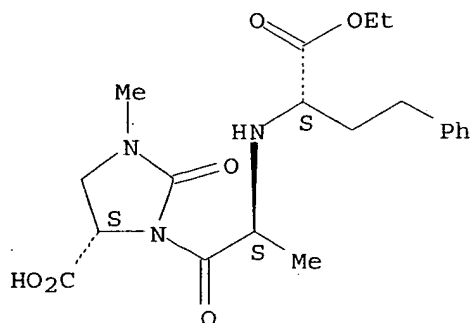
IT 50-28-2, 17 $\beta$ -Estradiol, biological studies 51-43-4, Epinephrine 60-80-0, Antipyrin 67-97-0, Vitamin D3 89371-37-9, Imidapril  
 RL: BIOL (Biological study)  
 (transdermal pharmaceuticals containing, fatty acid esters and alcs. in base for)

IT 89371-37-9, Imidapril  
 RL: BIOL (Biological study)  
 (transdermal pharmaceuticals containing, fatty acid esters and alcs. in base for)

RN 89371-37-9 HCAPLUS

CN 4-Imidazolidinecarboxylic acid, 3-[(2S)-2-[[[(1S)-1-(ethoxycarbonyl)-3-phenylpropyl]amino]-1-oxopropyl]-1-methyl-2-oxo-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L264 ANSWER 28 OF 63 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1992:639842 HCAPLUS

DOCUMENT NUMBER: 117:239842

TITLE: Transdermal compositions containing high concentration of active agents

INVENTOR(S): Taylor, Reginald Morton; Wilson, David John

PATENT ASSIGNEE(S): Commonwealth Scientific and Industrial Research Organization, Australia

SOURCE: PCT Int. Appl., 38 pp.  
 CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9214442	A1	19920903	WO 1992-AU58	19920218
W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE, US				
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG				
US 5308621	A	19940503	US 1991-795499	19911121
CA 2103725	AA	19920819	CA 1992-2103725	19920218
CA 2103725	C	20020604		
AU 9212723	A1	19920915	AU 1992-12723	19920218
AU 668679	B2	19960516		

EP 572494	A1	19931208	EP 1992-905485	19920218
EP 572494	B1	19990825		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL				
JP 06508100	T2	19940914	JP 1992-504787	19920218
AT 183639	E	19990915	AT 1992-905485	19920218
PRIORITY APPLN. INFO.:			AU 1991-4651	A 19910218
			AU 1991-7846	A 19910819
			AU 1991-7847	A 19910819
			AU 1991-7848	A 19910819
			US 1991-795499	A 19911121
			WO 1992-AU58	A 19920218

AB The title composition comprises a biol. active agent at a concentration above its

solubility limit in a carrier at ambient conditions, wherein there are sufficient fine particles of the agent dispersed through the carrier to facilitate the transdermal transfer capacity of the composition. For example, a composition containing ibuprofen (I), glycerol 26.2, propylene glycol 21.6, and polyethylene glycol 2.5g was prepared. The particle size of I in the

composition

was much smaller than that of I in a com. available cream.

IC ICM A61K009-10

ICS A61K009-06; A61K031-375; A61K031-19; A61K031-40

CC 63-6 (Pharmaceuticals)

IT Carboxylic **acids**, biological studies

RL: BIOL (Biological study)

(aryl, as nonsteroidal anti-inflammatory agents, transdermal compns. containing)

IT Carboxylic **acids**, biological studies

RL: BIOL (Biological study)

(heteroaryl, as nonsteroidal anti-inflammatory agents, transdermal compns. containing)

IT **Pharmaceutical dosage forms**

(transdermal, biol. active agents at excess solubility limit in, carriers for)

IT 9015-82-1, ACE

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(**inhibitors**, transdermal compns. containing)

IT 9015-82-1, ACE

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(**inhibitors**, transdermal compns. containing)

RN 9015-82-1 HCAPLUS

CN Carboxypeptidase, dipeptidyl, A (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

L264 ANSWER 29 OF 63

MEDLINE on STN

DUPLICATE 1

ACCESSION NUMBER: 2006068013 MEDLINE

DOCUMENT NUMBER: PubMed ID: 16451744

TITLE: Design, synthesis and characterization of captopril **prodrugs** for enhanced percutaneous absorption.

AUTHOR: Moss Gary P; Gullick Darren R; Cox Paul A; Alexander Cameron; Ingram Matthew J; Smart John D; Pugh W John

CORPORATE SOURCE: School of Pharmacy, University of Hertfordshire, College Lane, Hatfield, Hertfordshire AL10 9AB, UK..  
g.p.j.moss@herts.ac.uk

SOURCE: The Journal of pharmacy and pharmacology, (2006 Feb) Vol. 58, No. 2, pp. 167-77.

JOURNAL code: 0376363. ISSN: 0022-3573.  
PUB. COUNTRY: England: United Kingdom  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200604  
ENTRY DATE: Entered STN: 3 Feb 2006  
Last Updated on STN: 28 Apr 2006  
Entered Medline: 27 Apr 2006

## ABSTRACT:

Most drugs are designed primarily for oral administration, but the activity and stability profiles desirable for this route often make them unsuitable for transdermal delivery. We were therefore interested in designing analogues of captopril, a model drug with poor percutaneous penetration, for which the sustained steady-state blood plasma level associated with transdermal delivery (and which is unattainable orally) would be particularly beneficial. Quantitative structure-permeability relationships (QSPRs) predicted that \*\*\*ester\*\*\* and thiol **prodrug** derivatives of captopril would have lower maximal transdermal flux ( $J(m)$ ) than the parent drug, since the increases in permeability coefficient ( $k(p)$ ) of **prodrugs** would be outweighed by the reductions in aqueous solubility. Therefore, the aim of this study was to synthesize a series of **prodrugs** of captopril and to determine if a QSPR model could be used to design therapeutically viable **prodrugs**. Molecules with the highest predicted  $k(p)$  values were synthesized and characterized, and  $J(m)$  measured in Franz diffusion cells from saturated aqueous donor across porcine skin (fresh and frozen). In-vitro metabolism was also measured. Captopril and the **prodrugs** crossed the skin relatively freely, with  $J(m)$  being highest for ethyl to butyl **esters**. Substantial first-order metabolism of the **prodrugs** was observed, suggesting that their enhanced percutaneous absorption was complemented by their metabolic performance. The results suggested that QSPR models provided excellent enhancements in drug delivery. This was not seen at higher lipophilicities, suggesting that issues of solubility need to be considered in conjunction with any such use of a QSPR model.

CONTROLLED TERM: Administration, Cutaneous  
Animals  
\*Captopril  
Captopril: CH, chemistry  
Captopril: ME, metabolism  
Diffusion  
\*Dimethylpolysiloxanes: CH, chemistry  
Drug Design  
\*Esters  
Esters: CS, chemical synthesis  
Esters: ME, metabolism  
In Vitro  
Models, Biological  
\*Prodrugs  
Prodrugs: CS, chemical synthesis  
Prodrugs: ME, metabolism  
Quantitative Structure-Activity Relationship  
Research Support, Non-U.S. Gov't  
\*Silicones: CH, chemistry  
\*Skin: ME, metabolism  
\*Skin Absorption  
Swine  
CAS REGISTRY NO.: 62571-86-2 (Captopril); 63148-62-9 (baysilon)  
CHEMICAL NAME: 0 (Dimethylpolysiloxanes); 0 (Esters); 0 (Prodrugs); 0 (Silicones)

L264 ANSWER 30 OF 63 MEDLINE on STN DUPLICATE 2  
 ACCESSION NUMBER: 2004437128 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 15342185  
 TITLE: The effect of **penetration enhancers** on  
 drug delivery through skin: a QSAR study.  
 AUTHOR: Ghafourian Taravat; Zandasrar Parinaz; Hamishekar Hamed;  
 Nokhodchi Ali  
 CORPORATE SOURCE: School of Pharmacy, Tabriz University of Medical Sciences,  
 Tabriz 51664, Iran.. t.ghafourian@livjm.ac.uk  
 SOURCE: Journal of controlled release : official journal of the  
 Controlled Release Society, (2004 Sep 14) Vol. 99, No. 1,  
 pp. 113-25.  
 Journal code: 8607908. ISSN: 0168-3659.  
 PUB. COUNTRY: Netherlands  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 200503  
 ENTRY DATE: Entered STN: 3 Sep 2004  
 Last Updated on STN: 5 Mar 2005  
 Entered Medline: 4 Mar 2005

## ABSTRACT:

Skin **penetration enhancers** are used to allow formulation of transdermal delivery systems for drugs that are otherwise insufficiently skin-permeable. A full understanding of the mode of action could be beneficial for the design of potent enhancers and for the choice of the enhancer to be used in the topical formulation of a special drug. In this study, the structural requirements of **penetration enhancers** have been investigated using the Quantitative Structure-Activity Relationship (QSAR) technique. Activities of naturally occurring terpenes, pyrrolidinone and N-acetylproline derivatives on the skin penetration of 5-fluorouracil, diclofenac sodium (DFS), hydrocortisone (HC), estradiol and benazepril have been considered. The resulting QSARs indicated that for 5-fluorouracil and diclofenac sodium, less hydrophobic enhancers were the most active. More precisely, molecular descriptors in the corresponding QSARs indicated the possible involvement of intermolecular electron donor-acceptor interactions. This was in contrast to the skin permeation promotion of hydrocortisone, estradiol and benazepril by enhancers, where a linear relationship between enhancement activity and n-octanol/water partition coefficients of enhancers was evident. The possible mechanisms of **penetration**

\*\*\*enhancement\*\*\* as suggested by the QSARs will be discussed.

CONTROLLED TERM: \*Administration, Cutaneous  
 Animals  
 Benzazepines: AD, administration & dosage  
 Diclofenac: AD, administration & dosage  
 Estradiol: AD, administration & dosage  
 Fluorouracil: AD, administration & dosage  
 Humans  
 Hydrocortisone: AD, administration & dosage  
 In Vitro  
 Mice  
 Mice, Inbred HRS  
 Molecular Structure  
 \*Proline: AA, analogs & derivatives  
 Proline: CH, chemistry  
 Proline: PD, pharmacology  
 Pyrrolidinones: CH, chemistry  
 \*Pyrrolidinones: PD, pharmacology  
 \*Skin Absorption: DE, drug effects  
 Structure-Activity Relationship

Terpenes: CH, chemistry  
 \*Terpenes: PD, pharmacology  
 CAS REGISTRY NO.: 147-85-3 (Proline); 15307-86-5 (Diclofenac); 50-23-7 (Hydrocortisone); 50-28-2 (Estradiol); 51-21-8 (Fluorouracil); 86541-75-5 (**benazepril**)  
 CHEMICAL NAME: 0 (Benzazepines); 0 (Pyrrolidinones); 0 (Terpenes)

L264 ANSWER 31 OF 63 MEDLINE on STN DUPLICATE 4  
 ACCESSION NUMBER: 2002035158 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 11763476  
 TITLE: Effects of **adhesives** and **permeation enhancers** on the skin permeation of captopril.  
 AUTHOR: Park E S; Chang S J; Rhee Y S; Chi S C  
 CORPORATE SOURCE: College of Pharmacy, Sungkyunkwan University, Suwon, Korea.  
 SOURCE: Drug development and industrial pharmacy, (2001 Oct) Vol. 27, No. 9, pp. 975-80.  
 Journal code: 7802620. ISSN: 0363-9045.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 200205  
 ENTRY DATE: Entered STN: 24 Jan 2002  
 Last Updated on STN: 14 May 2002  
 Entered Medline: 13 May 2002

## ABSTRACT:

To formulate a transdermal drug delivery system of captopril, monolithic \*\*\*adhesive\*\*\* **matrix** type **patches** containing 20% captopril, different pressure-sensitive **adhesives**, and various \*\*\*permeation\*\*\* **enhancers** were prepared using a labcoater. The effects of the **adhesives** and **permeation enhancers** on skin permeation of captopril from the prepared **patches** were evaluated using Franz diffusion cells fitted with excised rat skins. The permeation rate of the drug through the excised skin was dependent on the type of polyacrylate copolymers studied. Fatty alcohols resulted in a pronounced enhancing effect on the skin permeation of captopril, while dimethyl sulfoxide, N-methyl-2-pyrrolidone, oleic acid, Transcutol, and polysorbate 20 showed no significant enhancing effect. The **permeation-\*\*\*enhancing\*\*\*** effect of the fatty alcohols reached the maximum at the level of 100%. **Based** on these results, a captopril **patch** may be developed with further optimization.

CONTROLLED TERM: Check Tags: Male  
 Acrylates  
 Adhesives  
 Administration, Cutaneous  
 Angiotensin-Converting Enzyme Inhibitors: AD, administration & dosage  
 \*Angiotensin-Converting Enzyme Inhibitors: PK, pharmacokinetics  
 Animals  
 Captopril: AD, administration & dosage  
 \*Captopril: PK, pharmacokinetics  
 Chromatography, High Pressure Liquid  
 Drug Delivery Systems  
 Excipients  
 Fatty Alcohols: PD, pharmacology  
 In Vitro  
 Rats  
 Rats, Sprague-Dawley  
 \*Skin Absorption: DE, drug effects

CAS REGISTRY NO.: 62571-86-2 (Captopril)  
CHEMICAL NAME: 0 (Acrylates); 0 (**Adhesives**); 0  
(Angiotensin-Converting Enzyme Inhibitors); 0 (Excipients);  
0 (Fatty Alcohols)

L264 ANSWER 32 OF 63 MEDLINE on STN DUPLICATE 5  
ACCESSION NUMBER: 96158395 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 8593260  
TITLE: Lyophilized aqueous based polymer  
matrices for transdermal delivery of captopril.  
AUTHOR: Dubey B K; Katare O P; Singh R; Jain S K  
CORPORATE SOURCE: Department of Pharmaceutical Sciences, Dr. Harisingh Gour  
Vishwavidyalaya, Sagar (M.P.), India.  
SOURCE: Journal of dermatological science, (1995 Nov) Vol. 10, No.  
3, pp. 191-5.  
Journal code: 9011485. ISSN: 0923-1811.  
PUB. COUNTRY: Ireland  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199604  
ENTRY DATE: Entered STN: 22 Apr 1996  
Last Updated on STN: 22 Apr 1996  
Entered Medline: 9 Apr 1996

## ABSTRACT:

Transdermal system(s) bearing captopril were developed using a low temperature casting method and aqueous based polymers viz., eudragit RL-100 and polyvinyl pyrrolidone (PVP). The developed system(s) were subjected to an in vitro characterization study. The results were compared with the transdermal systems of the same composition prepared at room temperature. The study revealed that the system(s) prepared using the low temperature casting method performed better in comparison to those prepared at room temperature. The developed system(s) followed zero order release kinetics.

CONTROLLED TERM: Acrylic Resins  
Administration, Cutaneous  
Cadaver  
\*Captopril: AD, administration & dosage  
Captopril: PK, pharmacokinetics  
Drug Delivery Systems  
Freeze Drying  
Humans  
Permeability  
Polymers  
Povidone  
Skin: ME, metabolism

CAS REGISTRY NO.: 33434-24-1 (Eudragit RS); 62571-86-2 (Captopril); 9003-39-8  
(Povidone)  
CHEMICAL NAME: 0 (Acrylic Resins); 0 (Polymers)

L264 ANSWER 33 OF 63 MEDLINE on STN  
ACCESSION NUMBER: 2001191607 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 11198612  
TITLE: Treatment of chronic hypertension with intravenous  
enalaprilat and transdermal clonidine.  
AUTHOR: Zawaideh M A; Duncan B; Joseph M W; Dixit M P  
CORPORATE SOURCE: Section of Pediatric Nephrology, Arizona Health Sciences  
Center, University of Arizona, 1501, N. Campbell Avenue,  
P.O. Box 245073, Tucson, AZ 85724, USA.  
SOURCE: Pediatric nephrology (Berlin, Germany), (2001 Jan) Vol. 16,  
No. 1, pp. 85-6.

JOURNAL CODE: 8708728. ISSN: 0931-041X.  
PUB. COUNTRY: Germany: Germany, Federal Republic of  
DOCUMENT TYPE: (CASE REPORTS)  
Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200104  
ENTRY DATE: Entered STN: 10 Apr 2001  
Last Updated on STN: 10 Apr 2001  
Entered Medline: 5 Apr 2001

## ABSTRACT:

We report an 11-year-old boy with hypertension and chronic intestinal pseudo-obstruction, which renders him totally dependent on parenteral nutrition and prevents the use of oral medications. Here we report the feasibility of utilizing chronic i.v. enalaprilat and transdermal clonidine on a chronic basis to control hypertension. Over the last 10 months, the patient's hypertension has been well controlled by 1.25 mg i.v. enalaprilat every 8 h and a 0.2-mg clonidine **patch** every 6 days, with no apparent side-effects. There are no reports of i.v. enalaprilat usage exceeding 3 weeks' duration. Therefore we believe that it is possible to effect reasonable management of chronic hypertension with the use of chronic i.v. enalaprilat and transdermal clonidine therapy.

CONTROLLED TERM: Check Tags: Male  
Administration, Cutaneous  
Adult  
\*Angiotensin-Converting Enzyme Inhibitors: AD,  
administration & dosage  
Angiotensin-Converting Enzyme Inhibitors: TU,  
therapeutic use  
\*Antihypertensive Agents: AD, administration & dosage  
Antihypertensive Agents: TU, therapeutic use  
Chronic Disease  
\*Clonidine: AD, administration & dosage  
Clonidine: TU, therapeutic use  
Drug Therapy, Combination  
\*Enalaprilat: AD, administration & dosage  
Enalaprilat: TU, therapeutic use  
Feasibility Studies  
Humans  
Hypertension: CO, complications  
\*Hypertension: DT, drug therapy  
Injections, Intravenous  
Intestinal Pseudo-Obstruction: CO, complications  
Intestinal Pseudo-Obstruction: TH, therapy  
Parenteral Nutrition  
CAS REGISTRY NO.: 4205-90-7 (Clonidine); 84680-54-6 (Enalaprilat)  
CHEMICAL NAME: 0 (Angiotensin-Converting Enzyme Inhibitors); 0  
(Antihypertensive Agents)

L264 ANSWER 34 OF 63 MEDLINE on STN  
ACCESSION NUMBER: 1998272062 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 9610531  
TITLE: Transdermal nitroglycerin **patch** therapy improves  
left ventricular function and prevents remodeling after  
acute myocardial infarction: results of a multicenter  
prospective randomized, double-blind, placebo-controlled  
trial.  
AUTHOR: Mahmarian J J; Moye L A; Chinoy D A; Sequeira R F; Habib G  
B; Henry W J; Jain A; Chaitman B R; Weng C S;  
Morales-Ballejo H; Pratt C M

CORPORATE SOURCE: Baylor College of Medicine, Houston, Tex, USA..  
johnj@bcm.tmc.edu  
SOURCE: Circulation, (1998 May 26) Vol. 97, No. 20, pp. 2017-24.  
Journal code: 0147763. ISSN: 0009-7322.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: (CLINICAL TRIAL)  
Journal; Article; (JOURNAL ARTICLE)  
(MULTICENTER STUDY)  
(RANDOMIZED CONTROLLED TRIAL)  
LANGUAGE: English  
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals  
ENTRY MONTH: 199806  
ENTRY DATE: Entered STN: 18 Jun 1998  
Last Updated on STN: 18 Jun 1998  
Entered Medline: 11 Jun 1998

## ABSTRACT:

BACKGROUND: Nitrates are widely used in the treatment of angina in patients with acute myocardial infarction (AMI). Short-term administration prevents left ventricular (LV) dilation and infarct expansion. However, little information is available regarding their long-term effects on LV remodeling in patients surviving Q-wave AMI. METHODS AND RESULTS: This was a randomized, double-blind, placebo-controlled trial designed to investigate the long-term (6-month) efficacy of intermittent transdermal nitroglycerin (NTG) \*\*\*patches\*\*\* on LV remodeling in 291 survivors of AMI. Patients meeting entry criteria had **baseline** gated radionuclide angiography (RNA) followed by randomization to placebo or active NTG **patches** delivering 0.4-, 0.8-, or 1.6-mg/h. RNA was repeated at 6 months and 6.5 days after withdrawal of double-blind medication. The primary study end point was the change in end-systolic volume index (ESVI). Both ESVI and end-diastolic volume index (EDVI) were significantly reduced with 0.4-mg/h NTG **patches** (-11.4 and -11.6 mL/m<sup>2</sup>, respectively, P<.03). This beneficial effect was observed primarily in patients with a **baseline** LV ejection fraction < or =40% (deltaESVI, -31 mL/m<sup>2</sup>; deltaEDVI, -33 mL/m<sup>2</sup>; both P<.05) and only at the 0.4-mg/h dose. After NTG **patch** withdrawal, ESVI significantly increased but did not reach pretreatment values. CONCLUSIONS: Transdermal NTG \*\*\*patches\*\*\* prevent LV dilation in patients surviving AMI. The beneficial effects are limited to patients with depressed LV function and only at the lowest (0.4-mg/h) dose. Continued administration is necessary to maintain efficacy. Whether these remodeling effects confer a clinical or survival advantage will need to be addressed in an adequately powered cardiac event trial.

CONTROLLED TERM: Check Tags: Female; Male  
Administration, Cutaneous  
Adult  
Aged  
Angiotensin-Converting Enzyme Inhibitors: TU,  
therapeutic use  
Cardiac Volume: DE, drug effects  
Double-Blind Method  
Humans  
Middle Aged  
\*Myocardial Infarction: DT, drug therapy  
Myocardial Infarction: PP, physiopathology  
\*Nitroglycerin: AD, administration & dosage  
Prospective Studies  
Research Support, Non-U.S. Gov't  
\*Vasodilator Agents: AD, administration & dosage  
\*Ventricular Function, Left: DE, drug effects  
CAS REGISTRY NO.: 55-63-0 (Nitroglycerin)  
CHEMICAL NAME: 0 (Angiotensin-Converting Enzyme Inhibitors); 0

## (Vasodilator Agents)

L264 ANSWER 35 OF 63 MEDLINE on STN  
 ACCESSION NUMBER: 1998288592 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 9626903  
 TITLE: Preventive effects of angiotensin-converting enzyme inhibitors on nitrate tolerance during continuous transdermal application of nitroglycerin in patients with chronic heart failure.  
 AUTHOR: Watanabe H; Kakihana M; Ohtsuka S; Sugishita Y  
 CORPORATE SOURCE: Department of Cardiology, KINU Medical Association Hospital, Mitsukaido, Ibaraki, Japan.  
 SOURCE: Japanese circulation journal, (1998 May) Vol. 62, No. 5, pp. 353-8.  
 Journal code: 7806868. ISSN: 0047-1828.  
 PUB. COUNTRY: Australia  
 DOCUMENT TYPE: (CLINICAL TRIAL)  
 Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199808  
 ENTRY DATE: Entered STN: 20 Aug 1998  
 Last Updated on STN: 20 Aug 1998  
 Entered Medline: 12 Aug 1998

## ABSTRACT:

This study was designed to investigate the effect of angiotensin-converting enzyme (ACE) inhibitors with and without a sulfhydryl group on intracellular production of cGMP, forearm blood flow, and neurohormonal factors during continuous transdermal application of nitroglycerin in patients with chronic heart failure. Platelet cGMP level and forearm blood flow were measured before and 5 min after sublingual administration of nitroglycerin (NTG) in 20 patients with chronic heart failure during the following 4 phases: (1) **baseline** phase; (2) NTG phase (1 week after NTG tape 10 mg/day); (3) CPT phase (1 week after both captopril 37.5 mg/day and NTG tape 10 mg/day); and (4) ENL phase (1 week after both enalapril 5 mg/day and NTG tape 10 mg/day). The platelet GMP level before sublingual NTG and forearm blood flow were significantly higher during the 3 phases with NTG tape than during the control phase. The percent increases in platelet cGMP level and forearm blood flow after sublingual NTG were significantly lower during the NTG phase than during the **baseline** phase. In contrast, concomitant application of ACE inhibitors maintained the percent increase in platelet cGMP level and forearm blood flow. These results indicate that concomitant therapy with ACE inhibitors may be helpful in preventing the attenuation of intracellular cGMP production in patients with chronic heart failure during continuous transdermal application of NTG.

CONTROLLED TERM: Check Tags: Female; Male

Administration, Cutaneous

Aged

\*Angiotensin-Converting Enzyme Inhibitors: PD, pharmacology

Atrial Natriuretic Factor: BL, blood

Atrial Natriuretic Factor: DE, drug effects

Blood Platelets: CH, chemistry

Blood Platelets: DE, drug effects

Blood Platelets: ME, metabolism

Blood Pressure: DE, drug effects

Body Weight: DE, drug effects

Chronic Disease

Cyclic GMP: BL, blood

Drug Tolerance

Forearm: BS, blood supply

\*Heart Failure, Congestive: DT, drug therapy  
 Heart Rate: DE, drug effects  
 Hematocrit  
 Humans  
 Middle Aged  
 \*Nitrates: PD, pharmacology  
 Nitroglycerin: AD, administration & dosage  
 \*Nitroglycerin: TU, therapeutic use  
 Norepinephrine: BL, blood  
 Regional Blood Flow: DE, drug effects  
 Renin: BL, blood  
 Renin: DE, drug effects  
 Systole  
 Vasodilator Agents: AD, administration & dosage  
 \*Vasodilator Agents: TU, therapeutic use  
 CAS REGISTRY NO.: 51-41-2 (Norepinephrine); 55-63-0 (Nitroglycerin);  
 7665-99-8 (Cyclic GMP); 85637-73-6 (Atrial Natriuretic  
 Factor)  
 CHEMICAL NAME: 0 (Angiotensin-Converting Enzyme Inhibitors); 0 (Nitrates);  
 0 (Vasodilator Agents); EC 3.4.23.15 (Renin)

L264 ANSWER 36 OF 63 MEDLINE on STN  
 ACCESSION NUMBER: 2004630142 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 15605449  
 TITLE: Percutaneous absorption of captopril from hydrophilic  
 cellulose derivatives through excised rabbit skin and human  
 skin.  
 AUTHOR: Wu P C; Huang Y B; Fang J Y; Tsai Y H  
 CORPORATE SOURCE: School of Pharmacy, Kaohsiung Medical College, 100 Shih  
 Chen 1st Rd., Kaohsiung 807, Taiwan, Republic of China.  
 SOURCE: Drug development and industrial pharmacy, (1998 Feb) Vol.  
 24, No. 2, pp. 179-82.  
 Journal code: 7802620. ISSN: 0363-9045.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 200501  
 ENTRY DATE: Entered STN: 21 Dec 2004  
 Last Updated on STN: 26 Jan 2005  
 Entered Medline: 25 Jan 2005

## ABSTRACT:

The purpose of this investigation was to evaluate the influence of percutaneous absorption of captopril from hydrophilic cellulose derivatives gel  
 \*\*\*bases\*\*\* (carboxymethylcellulose sodium [CMC], hydroxypropylcellulose [HPC] and hydroxylpropylmethylcellulose [HPMC]. The effects of various types and concentrations of **penetration enhancers** on captopril percutaneous absorption from HPC gel through rabbit skin were evaluated and selected to obtain some optimal formulations for penetration study through human chest skin. Then the required flux (1488 microg/hr) for captopril transdermal drug delivery system to maintain the therapeutic minimum effective concentration through human skin was used to evaluate the development of the optimal formulations. The results indicated that the minimum administered areas for therapeutic minimum effective concentration of captopril (cap) gel containing decanol (dec) were 10.4 cm<sup>2</sup> (5% cap, 7% dec) and 7.6 cm<sup>2</sup> (7% cap, 7% dec). These areas were within acceptable range, so these formulations can possibly be developed for a transdermal drug delivery system.

CONTROLLED TERM: Check Tags: Male  
 Administration, Cutaneous  
 Adult

\*Angiotensin-Converting Enzyme Inhibitors: AD,  
administration & dosage

Animals

\*Captopril: AD, administration & dosage

\*Chemistry, Pharmaceutical: MT, methods

Gels

Humans

Middle Aged

Rabbits

Research Support, Non-U.S. Gov't

Skin Absorption

CAS REGISTRY NO.: 62571-86-2 (Captopril)

CHEMICAL NAME: 0 (Angiotensin-Converting Enzyme Inhibitors); 0 (Gels)

L264 ANSWER 37 OF 63

MEDLINE on STN

ACCESSION NUMBER: 92268318 MEDLINE

DOCUMENT NUMBER: PubMed ID: 1587962

TITLE: Transdermal clonidine as an adjunct to enalapril: an  
evaluation of efficacy and patient compliance.

AUTHOR: Weidler D; Wallin J D; Cook E; Dillard D; Lewin A

CORPORATE SOURCE: Division of Clinical Pharmacology, University of Miami,  
Florida.

SOURCE: Journal of clinical pharmacology, (1992 May) Vol. 32, No.  
5, pp. 444-9.

Journal code: 0366372. ISSN: 0091-2700.

PUB. COUNTRY: United States

DOCUMENT TYPE: (CLINICAL TRIAL)

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199206

ENTRY DATE: Entered STN: 10 Jul 1992

Last Updated on STN: 10 Jul 1992

Entered Medline: 23 Jun 1992

ABSTRACT:

This four-center, 20-week, open-label study evaluated transdermal clonidine as an adjunct to enalapril 10 mg daily and demonstrated patterns of compliance. Seventy-four mildly to moderately hypertensive patients (mean seated blood pressure, 150/101 mm Hg) received enalapril 10 mg once daily as initial monotherapy. In 66 patients, the seated diastolic blood pressure remained greater than or equal to 90 mm Hg at the trough blood levels of enalapril. Transdermal clonidine (3.5 cm<sup>2</sup>, 7.0 cm<sup>2</sup>, or 10.5 cm<sup>2</sup>, equivalent to 0.1 mg, 0.2 mg, and 0.3 mg clonidine/day, respectively) then was added as needed to achieve blood pressure control. Forty-eight patients achieved diastolic blood pressures less than 90 mm Hg on concomitant therapy; 44 patients completed 8 weeks of maintenance dosing with a mean blood pressure of 134/85 mm Hg. Oral compliance, as measured by an electronic device that was actuated each time the medication vial was opened, varied from 48 to 140%. Compliance with the transdermal clonidine regimen was excellent; the **patch** was worn as directed during 96% of the patient-weeks of therapy. The authors conclude that blood pressure can be controlled by a combination of transdermal clonidine and enalapril in patients that do not adequately respond to enalapril monotherapy. Patients poorly complying with oral regimens may be candidates for a trial of transdermal clonidine monotherapy.

CONTROLLED TERM: Check Tags: Female; Male

Administration, Cutaneous

Adult

Aged

\*Clonidine: AD, administration & dosage

Clonidine: AE, adverse effects

Clonidine: PD, pharmacology  
Comparative Study  
Drug Therapy, Combination  
\*Enalapril: AD, administration & dosage  
Enalapril: AE, adverse effects  
Enalapril: PD, pharmacology

Humans

Middle Aged

Patient Compliance

CAS REGISTRY NO.: 4205-90-7 (Clonidine); 75847-73-3 (Enalapril)

L264 ANSWER 38 OF 63

MEDLINE on STN

ACCESSION NUMBER: 91191748 MEDLINE

DOCUMENT NUMBER: PubMed ID: 1901528

TITLE: Prevention of nitrate tolerance with angiotension converting enzyme inhibitors.

AUTHOR: Katz R J; Levy W S; Buff L; Wasserman A G

CORPORATE SOURCE: Department of Medicine, George Washington University, Washington, DC 20037.

SOURCE: Circulation, (1991 Apr) Vol. 83, No. 4, pp. 1271-7. Journal code: 0147763. ISSN: 0009-7322.

PUB. COUNTRY: United States

DOCUMENT TYPE: (CLINICAL TRIAL)

Journal; Article; (JOURNAL ARTICLE)

(RANDOMIZED CONTROLLED TRIAL)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 199105

ENTRY DATE: Entered STN: 2 Jun 1991

Last Updated on STN: 2 Jun 1991

Entered Medline: 14 May 1991

#### ABSTRACT:

**BACKGROUND.** Activation of neurohumoral hormones or sulfhydryl group depletion may contribute to the development of nitroglycerin tolerance. In an attempt to prevent nitrate tolerance, this study evaluated the interaction of nitroglycerin with angiotensin converting enzyme (ACE) inhibitors with and without a sulfhydryl group. **METHODS AND RESULTS.** Thirty-four subjects were randomized to a 7-day regimen of enalapril 10 mg b.i.d., captopril 25 mg t.i.d., or placebo. Venodilator response to nitroglycerin was assessed with forearm plethysmography by measuring the change in venous volume after administration of 0.4 mg sublingual nitroglycerin. Plethysmographic measurements were obtained serially 1) at **baseline**, 2) after 4 days of ACE inhibitor or placebo, 3) 2 hours after application of a 10 mg/24 hr nitroglycerin **patch**, and 4) 74 hours after continuous nitropatch application. ACE inhibition alone caused no significant change in the response to sublingual nitroglycerin. Nitrate response remained unchanged after 2 hours ("acute") of nitropatch exposure in all three groups. After 74 hours ("chronic") of continuous nitropatch application, the venodilator response to sublingual nitroglycerin was reduced by 40% in the placebo group, 10% in the enalapril group, and 2% in the captopril group. This attenuation was significant only in the placebo group (p less than 0.01). Pairwise comparison of nitrate response between groups was significantly different between the captopril and placebo groups (p less than 0.01) and between the placebo and enalapril groups (p less than 0.05). Plasma renin levels increased equally in the enalapril and captopril groups. Body weight increased only in the placebo group, suggesting prevention of nitrate-induced volume expansion in the ACE inhibitor groups. **CONCLUSIONS.** This study demonstrates that ACE inhibitors may prevent nitrate tolerance to long-term nitrate therapy.

CONTROLLED TERM: Check Tags: Female; Male

Administration, Cutaneous

Adult

**\*Angiotensin-Converting Enzyme Inhibitors: PD,**  
**pharmacology****Captopril: PD, pharmacology**

Comparative Study

Drug Tolerance

**Enalapril: PD, pharmacology**

Forearm: BS, blood supply

Humans

Middle Aged

Nitroglycerin: AD, administration &amp; dosage

**\*Nitroglycerin: PD, pharmacology**

Plethysmography

Research Support, Non-U.S. Gov't

Vasodilation: DE, drug effects

CAS REGISTRY NO.: 55-63-0 (Nitroglycerin); 62571-86-2 (Captopril); 75847-73-3  
(Enalapril)

CHEMICAL NAME: 0 (Angiotensin-Converting Enzyme Inhibitors)

L264 ANSWER 39 OF 63

MEDLINE on STN

ACCESSION NUMBER: 90283982 MEDLINE

DOCUMENT NUMBER: PubMed ID: 2191779

TITLE: A double-blind comparison of transdermal clonidine and oral  
captopril in essential hypertension.

AUTHOR: McMahon F G; Jain A K; Vargas R; Fillingim J

CORPORATE SOURCE: Tulane University School of Medicine, New Orleans,  
Louisiana.SOURCE: Clinical therapeutics, (1990 Mar-Apr) Vol. 12, No. 2, pp.  
88-100.

Journal code: 7706726. ISSN: 0149-2918.

PUB. COUNTRY: United States

DOCUMENT TYPE: (CLINICAL TRIAL)

Journal; Article; (JOURNAL ARTICLE)

(RANDOMIZED CONTROLLED TRIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199007

ENTRY DATE: Entered STN: 24 Aug 1990

Last Updated on STN: 24 Aug 1990

Entered Medline: 24 Jul 1990

## ABSTRACT:

In a double-blind study, patients with mild essential hypertension were randomly assigned to treatment with transdermal clonidine or oral captopril. After a two- to three-week titration period, blood pressure decreased significantly from 146.3/95.4 to 134.7/85.1 mmHg in the 33 clonidine-treated patients and from 143.0/96.1 to 134.8/87.1 mmHg in the 35 captopril-treated patients; the mean daily doses were 0.2 mg (equivalent) of clonidine and 122.9 mg of captopril. After eight weeks of treatment, blood pressures were reduced to 132.9/85.2 mmHg in the clonidine group (n = 22) and 131.2/82.5 mmHg in the captopril group (n = 16). In black patients, blood pressure reductions were greater with clonidine than with captopril. Four patients were withdrawn from treatment because of side effects in the clonidine group and one in the captopril group. No between-group differences were found in the responses to a quality-of-life questionnaire completed before and after treatment. The clonidine **patches** were worn during 99% of patient-weeks of treatment; captopril was taken as directed during 64% of patient-weeks of treatment. It is concluded that transdermal clonidine is safe and effective and well accepted by hypertensive patients.

CONTROLLED TERM: Check Tags: Female; Male

**Administration, Cutaneous**

Adult  
 Blood Pressure: DE, drug effects  
   Captopril: AD, administration & dosage  
   Captopril: AE, adverse effects  
   \*Captopril: TU, therapeutic use  
 Clonidine: AD, administration & dosage  
 Clonidine: AE, adverse effects  
 \*Clonidine: TU, therapeutic use  
 Comparative Study  
 Double-Blind Method  
 Humans  
 \*Hypertension: DT, drug therapy  
 Hypertension: PP, physiopathology  
 Patient Compliance  
 Pulse: DE, drug effects  
 Quality of Life  
 Randomized Controlled Trials  
 CAS REGISTRY NO.: 4205-90-7 (Clonidine); 62571-86-2 (Captopril)

L264 ANSWER 40 OF 63 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2005415778 EMBASE  
 TITLE: The renin-angiotensin systems: Evolving pharmacological perspectives for cerebroprotection.  
 AUTHOR: Magy L.; Vincent F.; Faure S.; Messerli F.H.; Wang J.G.; Achard J.-M.; Fournier A.  
 CORPORATE SOURCE: A. Fournier, Service de Nephrologie, CHU d'Amiens, Amiens, France. Fournier.Albert@chu-amiens.fr  
 SOURCE: Current Pharmaceutical Design, (2005) Vol. 11, No. 25, pp. 3275-3291.  
 Refs: 145  
 ISSN: 1381-6128 CODEN: CPDEFP  
 COUNTRY: Netherlands  
 DOCUMENT TYPE: Journal; General Review  
 FILE SEGMENT: 003 Endocrinology  
                   005 General Pathology and Pathological Anatomy  
                   008 Neurology and Neurosurgery  
                   018 Cardiovascular Diseases and Cardiovascular Surgery  
                   030 Pharmacology  
                   037 Drug Literature Index  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ENTRY DATE: Entered STN: 6 Oct 2005  
                   Last Updated on STN: 6 Oct 2005

ABSTRACT: During the last 20 years, the renin-angiotensin system (RAS) has become an increasingly important focus of basic and clinical cardiovascular research. One main conceptual step forward was made with the discovery of a tissue RAS and the understanding of its critical pathophysiological role in atherogenesis and plaque destabilisation [1]. Major effort to find new strategies for blocking the RAS has produced new classes of drugs which were expected to be clinically important in the management of hypertension and heart failure. As landmark clinical studies have demonstrated that inhibition of the RAS significantly reduces morbidity and mortality from coronary heart disease, myocardial infarction and heart failure, the concept has rapidly emerged that blocking the RAS was the strategy of choice for preventing cardiovascular diseases [2]. More recently, basic research has however continuously extended our understanding of the complexity of the systemic and tissue RASs, that can no longer be viewed as one-way streets in which one single effector, angiotensin II acts solely through its major (AT1) receptor. Meanwhile, clinical trials have challenged the concept that blocking the RAS is the most

effective preventive strategy for all patients and all target organs [3]. Consistent with the recent understanding that the RAS encompasses a number of distinct effectors acting through different receptors to promote opposite effects, a growing body of basic and clinical evidence suggests that blunting the RAS is a double-edge sword, with beneficial effects counterbalanced by deleterious ones, resulting in a net effect that critically depends on the experimental conditions, or the clinical characteristics of the study population. Of particular clinical relevance, a number of clinical trials point to the somewhat provocative conclusion that beyond their blood pressure lowering effect antihypertensive drugs that decrease angiotensin II formation are less stroke protective than the ones that increase angiotensin levels [4]. This review focuses on the recent experimental evidence demonstrating that angiotensin II and its derivatives acting through the non-AT1 receptors are involved in protective mechanisms against cerebral ischaemia and discusses in the light of the recent large cardiovascular prevention trials the clinical relevance of this new concept. The perspective of a renewal of therapeutical strategies to optimise the prevention of target organ damage and perhaps even some of the diseases of ageing, such as loss of cognitive function is emphasised. .COPYRG.T. 2005 Bentham Science Publishers Ltd.

CONTROLLED TERM: Medical Descriptors:  
 \*renin angiotensin aldosterone system  
 \*brain protection  
 cardiovascular disease: DT, drug therapy  
 cardiovascular disease: ET, etiology  
 cardiovascular disease: PC, prevention  
 hypertension: DT, drug therapy  
 heart failure  
 morbidity  
 mortality  
 ischemic heart disease  
 heart infarction  
 primary prevention  
 pathophysiology  
 atherogenesis  
 drug efficacy  
 drug targeting  
 stroke: DT, drug therapy  
 stroke: PC, prevention  
 brain ischemia: DT, drug therapy  
 brain ischemia: PC, prevention  
 aging  
 cognitive defect  
 oxidative stress  
 protein function  
 blood pressure regulation  
 antihypertensive activity  
 low drug dose  
 drug potentiation  
 drug selectivity  
 dose response  
 pleiotropy  
 drug penetration  
 systematic review  
 human  
 nonhuman  
 clinical trial  
 meta analysis  
 review  
 priority journal

## CONTROLLED TERM:

## Drug Descriptors:

angiotensin: EC, endogenous compound  
 angiotensin 1 receptor: EC, endogenous compound  
 antihypertensive agent: CT, clinical trial  
 antihypertensive agent: CB, drug combination  
 antihypertensive agent: CM, drug comparison  
 antihypertensive agent: DO, drug dose  
 antihypertensive agent: IT, drug interaction  
 antihypertensive agent: DT, drug therapy  
 antihypertensive agent: PK, pharmacokinetics  
 antihypertensive agent: PD, pharmacology  
 antihypertensive agent: CV, intracerebroventricular drug administration  
 antihypertensive agent: SC, subcutaneous drug administration  
 antihypertensive agent: TP, topical drug administration  
 angiotensin III: EC, endogenous compound  
 angiotensin II [3-8]: EC, endogenous compound  
 angiotensin[1-7]: DO, drug dose  
 angiotensin[1-7]: DT, drug therapy  
 angiotensin[1-7]: EC, endogenous compound  
 angiotensin[1-7]: PD, pharmacology  
 angiotensin 2 receptor: EC, endogenous compound  
 microsomal aminopeptidase: EC, endogenous compound  
 glutamyl aminopeptidase: EC, endogenous compound  
 membrane metalloendopeptidase: EC, endogenous compound  
 dipeptidyl carboxypeptidase: EC, endogenous compound  
 losartan: CT, clinical trial  
 losartan: CM, drug comparison  
 losartan: DT, drug therapy  
 losartan: PD, pharmacology  
 losartan: CV, intracerebroventricular drug administration  
 losartan: SC, subcutaneous drug administration  
 candesartan: CB, drug combination  
 candesartan: DO, drug dose  
 candesartan: IT, drug interaction  
 candesartan: DT, drug therapy  
 candesartan: PK, pharmacokinetics  
 candesartan: PD, pharmacology  
 nicotinoyltyrosyl(n benzyloxycarbonylarginyl)lysylhistidylprolylisoleucine: CB, drug combination  
 nicotinoyltyrosyl(n benzyloxycarbonylarginyl)lysylhistidylprolylisoleucine: CM, drug comparison  
 nicotinoyltyrosyl(n benzyloxycarbonylarginyl)lysylhistidylprolylisoleucine: IT, drug interaction  
 nicotinoyltyrosyl(n benzyloxycarbonylarginyl)lysylhistidylprolylisoleucine: DT, drug therapy  
 nicotinoyltyrosyl(n benzyloxycarbonylarginyl)lysylhistidylprolylisoleucine: PD, pharmacology  
 1 (4 dimethylamino 3 methylbenzyl) 5 diphenylacetyl 4,5,6,7 tetrahydro 1h imidazo[4,5 c]pyridine 6 carboxylic acid: CM, drug comparison  
 1 (4 dimethylamino 3 methylbenzyl) 5 diphenylacetyl 4,5,6,7 tetrahydro 1h imidazo[4,5 c]pyridine 6 carboxylic acid: DT, drug therapy  
 1 (4 dimethylamino 3 methylbenzyl) 5 diphenylacetyl 4,5,6,7 tetrahydro 1h imidazo[4,5 c]pyridine 6 carboxylic acid: PD, pharmacology  
 1 (4 dimethylamino 3 methylbenzyl) 5 diphenylacetyl 4,5,6,7 tetrahydro 1h imidazo[4,5 c]pyridine 6 carboxylic acid: SC,

subcutaneous drug administration  
lisinopril: CT, clinical trial  
lisinopril: CM, drug comparison  
lisinopril: DT, drug therapy  
lisinopril: PD, pharmacology  
dipeptidyl carboxypeptidase inhibitor: CT, clinical trial  
dipeptidyl carboxypeptidase inhibitor: CB, drug combination  
dipeptidyl carboxypeptidase inhibitor: CM, drug comparison  
dipeptidyl carboxypeptidase inhibitor: DT, drug therapy  
dipeptidyl carboxypeptidase inhibitor: PD, pharmacology  
**dipeptidyl carboxypeptidase inhibitor: TP, topical drug administration**  
angiotensin antagonist: CT, clinical trial  
angiotensin antagonist: CB, drug combination  
angiotensin antagonist: CM, drug comparison  
angiotensin antagonist: DO, drug dose  
angiotensin antagonist: IT, drug interaction  
angiotensin antagonist: DT, drug therapy  
angiotensin antagonist: PK, pharmacokinetics  
angiotensin antagonist: PD, pharmacology  
angiotensin antagonist: CV, intracerebroventricular drug administration  
angiotensin antagonist: SC, subcutaneous drug administration  
saralasin: CM, drug comparison  
saralasin: DT, drug therapy  
saralasin: PD, pharmacology  
enalaprilat: CM, drug comparison  
enalaprilat: DT, drug therapy  
enalaprilat: PD, pharmacology  
enalapril: CM, drug comparison  
enalapril: DT, drug therapy  
enalapril: PD, pharmacology  
captopril: CT, clinical trial  
captopril: CM, drug comparison  
captopril: DT, drug therapy  
captopril: PD, pharmacology  
**captopril: TP, topical drug administration**  
amastatin: PD, pharmacology  
irbesartan: DT, drug therapy  
irbesartan: PD, pharmacology  
irbesartan: CV, intracerebroventricular drug administration  
diuretic agent: CT, clinical trial  
diuretic agent: CB, drug combination  
diuretic agent: CM, drug comparison  
diuretic agent: IT, drug interaction  
diuretic agent: DT, drug therapy  
diuretic agent: PD, pharmacology  
beta adrenergic receptor blocking agent: CT, clinical trial  
beta adrenergic receptor blocking agent: CM, drug comparison  
beta adrenergic receptor blocking agent: DT, drug therapy  
beta adrenergic receptor blocking agent: PD, pharmacology  
perindopril: CT, clinical trial  
perindopril: CB, drug combination  
perindopril: CM, drug comparison  
perindopril: DT, drug therapy  
amlodipine: CT, clinical trial  
amlodipine: CM, drug comparison  
amlodipine: DT, drug therapy

ramipril: CT, clinical trial  
 ramipril: DT, drug therapy  
 unindexed drug

CAS REGISTRY NO.: (angiotensin) 11128-99-7, 1407-47-2; (angiotensin III) 12687-51-3; (angiotensin[1-7]) 39386-80-6; (microsomal aminopeptidase) 9054-63-1; (glutamyl aminopeptidase) 9074-83-3; (membrane metalloendopeptidase) 82707-54-8, 88201-55-2; (dipeptidyl carboxypeptidase) 9015-82-1; (losartan) 114798-26-4; (candesartan) 139481-59-7; (nicotinoyltyrosyl(n benzyloxycarbonylarginyl)lysylhistidyl prolylisoleucine) 127060-75-7; (1 (4 dimethylamino 3 methylbenzyl) 5 diphenylacetyl 4,5,6,7 tetrahydro 1h imidazo[4,5 c]pyridine 6 carboxylic acid) 130663-39-7; (lisinopril) 76547-98-3, 83915-83-7; (saralasin) 34273-10-4; (enalaprilat) 76420-72-9; (enalapril) 75847-73-3; (captopril) 62571-86-2; (amastatin) 67655-94-1; (irbesartan) 138402-11-6; (perindopril) 82834-16-0; (amlodipine) 88150-42-9; (ramipril) 87333-19-5

CHEMICAL NAME: Cgp 42112; Pd 123319; Cgp 42112a

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ACCESSION NUMBER: 2005201040 EMBASE  
 TITLE: Effect of CS-088, an angiotensin AT(1) receptor antagonist, on intraocular pressure in glaucomatous monkey eyes.  
 AUTHOR: Wang R.-F.; Podos S.M.; Mittag T.W.; Yokoyoma T.  
 CORPORATE SOURCE: Dr. R.-F. Wang, Department of Ophthalmology, Mt. Sinai Sch. Med. New York Univ., Box 1183, One Gustave L. Levy Place, New York, NY, United States. rong-fang.wang@mssm.edu  
 SOURCE: Experimental Eye Research, (2005) Vol. 80, No. 5, pp. 629-632.  
 Refs: 15  
 ISSN: 0014-4835 CODEN: EXERA6  
 COUNTRY: United Kingdom  
 DOCUMENT TYPE: Journal; Article  
 FILE SEGMENT: 012 Ophthalmology  
 030 Pharmacology  
 037 Drug Literature Index  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ENTRY DATE: Entered STN: 2 Jun 2005  
 Last Updated on STN: 2 Jun 2005

ABSTRACT: To evaluate the effect of CS-088, an angiotensin AT1 receptor antagonist, on intraocular pressure (IOP) in monkey eyes with unilateral laser-induced glaucoma. A multiple-dose study was performed in 8 glaucomatous monkey eyes. One 50 µl drop of CS-088, 2% or 4%, was topically applied to the glaucomatous eye at 9:30 a.m. and 3:30 p.m. for 5 consecutive days. IOP was measured hourly for 6 hours beginning at 9:30 a.m. for one baseline day, one vehicle-treated day, and daily for 5 days of treatment with CS-088. The washout period between the two drug concentrations was at least 2 weeks. Twice daily administration of 2% CS-088 for 5 days did not reduce the IOP until the third dose on day 2 of the treatment regimen. A significant ( $p < 0.02$ ) reduction in IOP began 1 hour after the third dose, and lasted for 3 hours. The maximum reduction in IOP was  $5.3 \pm 0.8$  (mean  $\pm$  SEM) mmHg (15%) ( $p < 0.001$ ), with the longest duration of IOP reduction of at least 6 hours after dosing on day 5. The 4% dose of CS-088 reduced ( $p < 0.05$ ) IOP from 1 to 5 hours after the first dose. The maximum reduction in IOP was  $6.9 \pm 1.0$  mmHg (20%), with the longest duration of IOP reduction of at least 18 hours after administration on day 5. Both 2% and 4% CS-088 showed enhancement of the ocular hypotensive effect with repeated dosing. 4% CS-088 produced greater ( $p < 0.05$ ) IOP reduction with longer

duration of action than 2%. Topically applied CS-088, a new antagonist drug at the angiotensin AT1 receptor, reduced IOP in glaucomatous monkey eyes in a dose-dependent manner. .COPYRGHT. 2004 Elsevier Ltd. All rights reserved.

CONTROLLED TERM: Medical Descriptors:  
 \*intraocular pressure  
 \*glaucoma: DT, drug therapy  
 monkey  
 eye  
 drug effect  
 laser  
 concentration response  
 reduction  
 hypotension  
 dose response  
 human  
 nonhuman  
 animal model  
 controlled study  
 animal tissue  
 animal cell  
 article  
 priority journal  
 Drug Descriptors:  
 \*angiotensin 1 receptor antagonist: CM, drug comparison  
 \*angiotensin 1 receptor antagonist: DT, drug therapy  
 \*angiotensin 1 receptor antagonist: PD, pharmacology  
 \*angiotensin 1 receptor antagonist: TP, topical drug  
 administration  
 timolol: CM, drug comparison  
 timolol: DT, drug therapy  
 timolol: PD, pharmacology  
 losartan potassium: DT, drug therapy  
 losartan potassium: PO, oral drug administration  
 losartan potassium: PD, pharmacology  
 dipeptidyl carboxypeptidase inhibitor: DT, drug therapy  
 dipeptidyl carboxypeptidase inhibitor: TP, topical drug  
 administration  
 enalaprilat: DT, drug therapy  
 enalaprilat: PD, pharmacology  
 enalaprilat: TP, topical drug administration  
 ramiprilat: DT, drug therapy  
     **ramiprilat: TP, topical drug administration**  
 fosinopril: DT, drug therapy  
     **fosinopril: TP, topical drug administration**  
 cs 088

CAS REGISTRY NO.: (timolol) 26839-75-8; (losartan potassium) 124750-99-8;  
 (enalaprilat) 76420-72-9; (ramiprilat) 87269-97-4;  
 (fosinopril) 88889-14-9, 98048-97-6

CHEMICAL NAME: Cs 088

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ACCESSION NUMBER: 2003055396 EMBASE  
 TITLE: Transdermal therapeutics.  
 AUTHOR: Marks S.L.; Taboada J.  
 CORPORATE SOURCE: S.L. Marks, Dept. of Veterinary Clinical Med., College of  
 Veterinary Medicine, University of Illinois, Urbana, IL  
 61821, United States  
 SOURCE: Journal of the American Animal Hospital Association, (2003)

Vol. 39, No. 1, pp. 19-21. .  
Refs: 20  
ISSN: 0587-2871 CODEN: JAAHBL  
COUNTRY: United States  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 030 Pharmacology  
037 Drug Literature Index  
039 Pharmacy  
052 Toxicology  
LANGUAGE: English  
ENTRY DATE: Entered STN: 20 Feb 2004  
Last Updated on STN: 20 Feb 2004  
CONTROLLED TERM: Medical Descriptors:  
\*drug administration route  
\*veterinary medicine  
skin function  
epidermis  
dermis  
stratum corneum  
drug absorption  
drug diffusion  
diffusion coefficient  
partition coefficient  
surface property  
body temperature  
body composition  
drug efficacy  
drug solubility  
drug stability  
first pass effect  
drug transformation  
hyperthyroidism: DI, diagnosis  
hyperthyroidism: DT, drug therapy  
drug blood level  
drug dose regimen  
transdermal patch  
article  
Drug Descriptors:  
thiamazole: AD, drug administration  
thiamazole: CR, drug concentration  
thiamazole: DT, drug therapy  
thiamazole: PD, pharmacology  
thiamazole: TD, transdermal drug administration  
amitriptyline: AD, drug administration  
amitriptyline: TD, transdermal drug administration  
buspirone: AD, drug administration  
buspirone: TD, transdermal drug administration  
diltiazem: AD, drug administration  
diltiazem: TD, transdermal drug administration  
ondansetron: AD, drug administration  
ondansetron: TD, transdermal drug administration  
glyceryl trinitrate: AD, drug administration  
glyceryl trinitrate: TD, transdermal drug administration  
fentanyl: AD, drug administration  
fentanyl: PR, pharmaceuticals  
fentanyl: TD, transdermal drug administration  
metoclopramide: AD, drug administration  
metoclopramide: CR, drug concentration  
metoclopramide: TD, transdermal drug administration  
propranolol: AD, drug administration

propranolol: PR, pharmaceuticals  
 propranolol: TD, transdermal drug administration  
 metronidazole: AD, drug administration  
 metronidazole: PR, pharmaceuticals  
 metronidazole: TD, transdermal drug administration  
 cefalexin: AD, drug administration  
 cefalexin: PR, pharmaceuticals  
 cefalexin: TD, transdermal drug administration  
 nifedipine: AD, drug administration  
 nifedipine: PR, pharmaceuticals  
 nifedipine: TD, transdermal drug administration  
 diclofenac: AD, drug administration  
 diclofenac: PR, pharmaceuticals  
 diclofenac: TD, transdermal drug administration  
 insulin: AD, drug administration  
 insulin: PR, pharmaceuticals  
 insulin: TD, transdermal drug administration  
 aminophylline: AD, drug administration  
 aminophylline: TD, transdermal drug administration  
 amoxicillin: AD, drug administration  
 amoxicillin: TD, transdermal drug administration  
 buprenorphine: AD, drug administration  
 buprenorphine: TD, transdermal drug administration  
 chloramphenicol: AD, drug administration  
 chloramphenicol: TD, transdermal drug administration  
 chlorpromazine: AD, drug administration  
 chlorpromazine: TD, transdermal drug administration  
 cisapride: AD, drug administration  
 cisapride: TD, transdermal drug administration  
 clindamycin: AD, drug administration  
 clindamycin: TD, transdermal drug administration  
 cyproheptadine: AD, drug administration  
 cyproheptadine: TD, transdermal drug administration  
 diphenhydramine: AD, drug administration  
 diphenhydramine: TD, transdermal drug administration  
 doxycycline: AD, drug administration  
 doxycycline: TD, transdermal drug administration  
 enalapril: AD, drug administration  
**enalapril: TD, transdermal drug administration**  
 enrofloxacin: AD, drug administration  
 enrofloxacin: TD, transdermal drug administration  
 famotidine: AD, drug administration  
 famotidine: TD, transdermal drug administration  
 furosemide: AD, drug administration  
 furosemide: TD, transdermal drug administration  
 dimethyl sulfoxide: TO, drug toxicity  
 unindexed drug

CAS REGISTRY NO.: (thiamazole) 60-56-0; (amitriptyline) 50-48-6, 549-18-8;  
 (buspirone) 33386-08-2, 36505-84-7; (diltiazem) 33286-22-5,  
 42399-41-7; (ondansetron) 103639-04-9, 116002-70-1,  
 99614-01-4; (glyceryl trinitrate) 55-63-0; (fentanyl)  
 437-38-7; (metoclopramide) 12707-59-4, 2576-84-3, 364-62-5,  
 7232-21-5; (propranolol) 13013-17-7, 318-98-9, 3506-09-0,  
 4199-09-1, 525-66-6; (metronidazole) 39322-38-8, 443-48-1;  
 (cefalexin) 15686-71-2, 23325-78-2; (nifedipine)  
 21829-25-4; (diclofenac) 15307-79-6, 15307-86-5; (insulin)  
 9004-10-8; (aminophylline) 317-34-0; (amoxicillin)  
 26787-78-0, 34642-77-8, 61336-70-7; (buprenorphine)  
 52485-79-7, 53152-21-9; (chloramphenicol) 134-90-7,  
 2787-09-9, 56-75-7; (chlorpromazine) 50-53-3, 69-09-0;

(cisapride) 81098-60-4; (clindamycin) 18323-44-9;  
 (ciproheptadine) 129-03-3, 969-33-5; (diphenhydramine)  
 147-24-0, 58-73-1; (doxycycline) 10592-13-9, 17086-28-1,  
 564-25-0; (enalapril) 75847-73-3; (enrofloxacin)  
 93106-60-6; (famotidine) 76824-35-6; (furosemide) 54-31-9;  
 (dimethyl sulfoxide) 67-68-5

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ACCESSION NUMBER: 2002053548 EMBASE  
 TITLE: Novel acrylate **adhesives** for transdermal drug delivery.  
 AUTHOR: Cantor A.S.; Wirtanen D.J.  
 CORPORATE SOURCE: Dr. A.S. Cantor, 3M Drug Delivery Systems Division, 3M Center, Building 260-4N-12, St. Paul, MN 55144-1000, United States. ascantor@mmm.com  
 SOURCE: Pharmaceutical Technology, (2002) Vol. 26, No. 1, pp. 28-38.  
 Refs: 8  
 ISSN: 0147-8087 CODEN: PTECDN  
 COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article  
 FILE SEGMENT: 027 Biophysics, Bioengineering and Medical Instrumentation  
 037 Drug Literature Index  
 039 Pharmacy  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ENTRY DATE: Entered STN: 21 Feb 2002  
 Last Updated on STN: 21 Feb 2002

ABSTRACT: In this article, the authors discuss novel acrylate **adhesive** polymers developed for use in transdermal drug delivery systems. They analyze the solubility and **adhesive** performances of **adhesives** that incorporate either hydroxyethyl acrylate (HEA) or pyrrolidonoethyl acrylate (PyEA) as a polar monomer to control drug solubility. A graft macromer is used to control **adhesive** performance. Testing of transdermal patches in human skin panel studies suggests that the macromer component may help reduce cold flow at the edges of the patch and also may reduce irritation.

CONTROLLED TERM: Medical Descriptors:  
 \*drug delivery system  
 drug solubility  
 transdermal patch  
 drug formulation  
 drug release  
 drug stability  
 human  
 human tissue  
 article  
 Drug Descriptors:  
 \*adhesive agent: AD, drug administration  
 \*adhesive agent: PR, pharmaceuticals  
 \*adhesive agent: TD, transdermal drug administration  
 \*acrylic acid derivative: AD, drug administration  
 \*acrylic acid derivative: PR, pharmaceuticals  
 \*acrylic acid derivative: TD, transdermal drug administration  
 copolymer  
 buprenorphine

cyproheptadine  
 phenobarbital  
 testosterone  
 captopril  
 haloperidol  
 morphine  
 atenolol: PR, pharmaceuticals  
 pyrrolidine derivative: PR, pharmaceuticals  
 octanoic acid: PR, pharmaceuticals  
 benzyl alcohol: PR, pharmaceuticals  
 glycerol derivative: PR, pharmaceuticals  
 dodecylamine: PR, pharmaceuticals

CAS REGISTRY NO.: (buprenorphine) 52485-79-7, 53152-21-9; (cyproheptadine) 129-03-3, 969-33-5; (phenobarbital) 50-06-6, 57-30-7, 8028-68-0; (testosterone) 58-22-0; (captopril) 62571-86-2; (haloperidol) 52-86-8; (morphine) 52-26-6, 57-27-2; (atenolol) 29122-68-7; (octanoic acid) 124-07-2, 1984-06-1, 74-81-7; (benzyl alcohol) 100-51-6; (dodecylamine) 124-22-1, 929-73-7

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ACCESSION NUMBER: 2001283059 EMBASE  
 TITLE: Potential and problems of developing transdermal patches for veterinary applications.  
 AUTHOR: Riviere J.E.; Papich M.G.  
 CORPORATE SOURCE: J.E. Riviere, Ctr. Cutan. Toxicol./Residue Pharma., College of Veterinary Medicine, North Carolina State University, Raleigh, NC 27613, United States. Jim\_Riviere@ncsu.edu  
 SOURCE: Advanced Drug Delivery Reviews, (1 Sep 2001) Vol. 50, No. 3, pp. 175-203.  
 Refs: 78  
 ISSN: 0169-409X CODEN: ADDREP  
 PUBLISHER IDENT.: S 0169-409X(01)00157-0  
 COUNTRY: Netherlands  
 DOCUMENT TYPE: Journal; Article  
 FILE SEGMENT: 037 Drug Literature Index  
 039 Pharmacy  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ENTRY DATE: Entered STN: 6 Sep 2001  
 Last Updated on STN: 6 Sep 2001

ABSTRACT: A new frontier in the administration of therapeutic drugs to veterinary species is transdermal drug delivery. The primary challenge in developing these systems is rooted in the wide differences in skin structure and function seen in species ranging from cats to cows. The efficacy of a transdermal system is primarily dependent upon the barrier properties of the targeted species skin, as well as the ratio of the area of the transdermal patch to the species total body mass needed to achieve effective systemic drug concentrations. A drug must have sufficient lipid solubility to traverse the epidermal barrier to be considered for delivery for this route. A number of insecticides have been developed in liquid 'pour-on' formulations that illustrate the efficacy of this route of administration for veterinary species. The human transdermal fentanyl patch has been successfully used in cats and dogs for post-operative analgesia. The future development of transdermal drug delivery systems for veterinary species will be drug and species specific. With efficient experimental designs and available transdermal patch technology, there are no obvious hurdles to the development of effective systems in many veterinary species. .COPYRGHT. 2001 Elsevier Science B.V. All rights reserved.

## CONTROLLED TERM:

## Medical Descriptors:

- \*transdermal patch
- \*drug delivery system
- \*parasitosis: DT, drug therapy
- \*animal disease
- skin function
- body mass
- skin penetration
- drug solubility
- drug penetration
- epidermis
- drug formulation
- species difference
- drug diffusion
- skin absorption
- nonhuman
- article
- priority journal

## Drug Descriptors:

- \*veterinary drug: DT, drug therapy
- \*veterinary drug: PR, pharmaceuticals
- \*veterinary drug: TP, topical drug administration
- \*pesticide: PR, pharmaceuticals
- \*pesticide: TP, topical drug administration
- fipronil: DT, drug therapy
- fipronil: PR, pharmaceuticals
- fipronil: TP, topical drug administration
- imadacloprid: DT, drug therapy
- imadacloprid: PR, pharmaceuticals
- imadacloprid: TP, topical drug administration
- selamectin: DT, drug therapy
- selamectin: PR, pharmaceuticals
- selamectin: TP, topical drug administration
- salbutamol: PR, pharmaceuticals
- salbutamol: TD, transdermal drug administration
- alprazolam: PR, pharmaceuticals
- alprazolam: TD, transdermal drug administration
- atenolol: PR, pharmaceuticals
- atenolol: TD, transdermal drug administration
- buprenorphine: PR, pharmaceuticals
- buprenorphine: TD, transdermal drug administration
- cytarabine: PR, pharmaceuticals
- cytarabine: TD, transdermal drug administration
- selegiline: PR, pharmaceuticals
- selegiline: TD, transdermal drug administration
- prasterone: PR, pharmaceuticals
- prasterone: TD, transdermal drug administration
- dronabinol: PR, pharmaceuticals
- dronabinol: TD, transdermal drug administration
- enalapril: PR, pharmaceuticals
- enalapril: TD, transdermal drug administration
- eptazocine: PR, pharmaceuticals
- eptazocine: TD, transdermal drug administration
- ethinylestradiol: PR, pharmaceuticals
- ethinylestradiol: TD, transdermal drug administration
- isosorbide dinitrate: PR, pharmaceuticals
- isosorbide dinitrate: TD, transdermal drug administration
- ketorolac trometamol: PR, pharmaceuticals
- ketorolac trometamol: TD, transdermal drug administration
- ketotifen: PR, pharmaceuticals

ketotifen: TD, transdermal drug administration  
ketoprofen: PR, pharmaceuticals  
ketoprofen: TD, transdermal drug administration  
norethisterone: PR, pharmaceuticals  
norethisterone: TD, transdermal drug administration  
prazosin: PR, pharmaceuticals  
prazosin: TD, transdermal drug administration  
terfenadine: PR, pharmaceuticals  
terfenadine: TD, transdermal drug administration  
chlorinated hydrocarbon: PR, pharmaceuticals  
chlorinated hydrocarbon: TP, topical drug administration  
organophosphate insecticide: PR, pharmaceuticals  
organophosphate insecticide: TP, topical drug administration  
carbamate insecticide: PR, pharmaceuticals  
carbamate insecticide: TP, topical drug administration  
pyrethroid: PR, pharmaceuticals  
pyrethroid: TP, topical drug administration  
anthelmintic agent: PR, pharmaceuticals  
anthelmintic agent: TP, topical drug administration  
unindexed drug  
unclassified drug

CAS REGISTRY NO.: (fipronil) 120068-37-3; (salbutamol) 18559-94-9;  
(alprazolam) 28981-97-7; (atenolol) 29122-68-7;  
(buprenorphine) 52485-79-7, 53152-21-9; (cytarabine)  
147-94-4, 69-74-9; (selegiline) 14611-51-9, 14611-52-0,  
2079-54-1, 2323-36-6; (prasterone) 53-43-0; (dronabinol)  
7663-50-5; (enalapril) 75847-73-3; (eptazocine) 72150-17-5,  
72522-13-5; (ethinylestradiol) 57-63-6; (isosorbide  
dinitrate) 87-33-2; (ketorolac trometamol) 74103-07-4;  
(ketotifen) 34580-13-7; (ketoprofen) 22071-15-4,  
57495-14-4; (norethisterone) 68-22-4; (prazosin)  
19216-56-9, 19237-84-4; (terfenadine) 50679-08-8

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ACCESSION NUMBER: 1998048174 EMBASE  
TITLE: Nitrates and left ventricular remodeling.  
AUTHOR: Jugdutt B.I.  
CORPORATE SOURCE: Dr. B.I. Jugdutt, Walter Mackenzie Health Sci. Centre,  
Department of Medicine, University of Alberta, Edmonton,  
Alta. T6G 2R7, Canada  
SOURCE: American Journal of Cardiology, (1998) Vol. 81, No. 1 A,  
pp. 57A-67A. .  
Refs: 140  
ISSN: 0002-9149 CODEN: AJCDAG  
PUBLISHER IDENT.: S00291499801000X  
COUNTRY: United States  
DOCUMENT TYPE: Journal; Conference Article  
FILE SEGMENT: 006 Internal Medicine  
018 Cardiovascular Diseases and Cardiovascular Surgery  
030 Pharmacology  
037 Drug Literature Index  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ENTRY DATE: Entered STN: 27 Feb 1998  
Last Updated on STN: 27 Feb 1998

ABSTRACT: Left ventricular remodeling is the major mechanism leading to cardiac enlargement, failure, and death after myocardial infarction. It is associated with early disruption of collagen matrix and expansion of

the infarct zone (IZ) followed by progressive global ventricular dilation, hypertrophy of the noninfarct zone (NIZ), and further global dysfunction. In parallel, it is associated with healing which repairs the IZ with collagenous scar. Mechanical deformation forces, including ventricular diastolic and systolic loads, mediate structural remodeling during healing, and beyond. Experimental and clinical evidence indicate that early and prolonged impedance reduction and diastolic unloading with nitric oxide donors like nitrates can effectively limit remodeling. Other benefits are mediated by limitation of infarct size and transmural flow, improvement of left ventricular hemodynamics and collateral flow, decreased reperfusion injury, and antithrombotic effects. In addition to these benefits, nitrates have nonhemodynamic, antigrowth and cellular actions that limit progressive remodeling after infarction.

CONTROLLED TERM: Medical Descriptors:  
 \*heart ventricle remodeling  
 \*heart infarction: DT, drug therapy  
 pathophysiology  
 heart infarction size  
 hemodynamics  
 survival rate  
 human  
 clinical trial  
 oral drug administration  
 intravenous drug administration  
**transdermal drug administration**  
 conference paper  
 priority journal  
 Drug Descriptors:  
 \*nitric acid derivative: CT, clinical trial  
 \*nitric acid derivative: CB, drug combination  
 \*nitric acid derivative: DT, drug therapy  
 \*vasodilator agent  
 \*antithrombotic agent  
 \*anticoagulant agent  
 \*captopril: CT, clinical trial  
 \*captopril: CB, drug combination  
 \*captopril: DT, drug therapy  
 placebo  
 isosorbide 5 nitrate: CT, clinical trial  
 isosorbide 5 nitrate: DT, drug therapy  
 glyceryl trinitrate: CT, clinical trial  
 glyceryl trinitrate: CB, drug combination  
 glyceryl trinitrate: DT, drug therapy  
 CAS REGISTRY NO.: (captopril) 62571-86-2; (isosorbide 5 nitrate) 16051-77-7;  
 (glyceryl trinitrate) 55-63-0

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ACCESSION NUMBER: 97043563 EMBASE

DOCUMENT NUMBER: 1997043563

TITLE: Percutaneous absorption of captopril from hydrophilic cellulose gel.RTM. through excised rabbit skin and human skin.

AUTHOR: Wu P.-C.; Huang Y.-B.; Lin H.-H.; Tsai Y.H.

CORPORATE SOURCE: Y.H. Tsai, School of Pharmacy, Kaohsiung Medical College, Kaohsiung, ROC, Taiwan, Province of China

SOURCE: International Journal of Pharmaceutics, (1996) Vol. 145, No. 1-2, pp. 215-220.

Refs: 14

ISSN: 0378-5173 CODEN: IJPHDE

PUBLISHER IDENT.: S 0378-5173(96)04773-4  
COUNTRY: Netherlands  
DOCUMENT TYPE: Journal; Article  
FILE SEGMENT: 013 Dermatology and Venereology  
018 Cardiovascular Diseases and Cardiovascular Surgery  
030 Pharmacology  
037 Drug Literature Index  
039 Pharmacy  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ENTRY DATE: Entered STN: 3 Mar 1997  
Last Updated on STN: 3 Mar 1997

ABSTRACT: The purpose of this investigation was to design and evaluate the percutaneous absorption of captopril from a hydrophilic cellulose gel \*\*\*base\*\*\*. The effect of type and concentration of saturated fatty acids, amount of gel base as well as the concentration of drug on percutaneous absorption of captopril gel through rabbit skin were evaluated and selected to obtain some optimal formulations. Then the required flux (1488 µg/h) for captopril transdermal drug delivery system to maintain the therapeutic minimum effective concentration through human skin was used to evaluate the development of the optimal formulations. The results indicated that these formulations containing 3, 5 and 10% captopril with 5% capric acid using 22.89, 6.98 and 4.89 cm<sup>2</sup> of administered area were attained to the therapeutic minimum effective concentration. Therefore these formulations were suitable for possible development of transdermal drug delivery system.

CONTROLLED TERM: Medical Descriptors:  
\*skin absorption  
animal tissue  
article  
controlled study  
drug release  
gel  
human  
human tissue  
in vitro study  
nonhuman  
normal human  
priority journal  
rabbit  
transdermal drug administration  
Drug Descriptors:  
\*captopril: AN, drug analysis  
\*captopril: CR, drug concentration  
\*captopril: DO, drug dose  
\*captopril: PR, pharmaceuticals  
\*captopril: PK, pharmacokinetics  
cellulose: CB, drug combination  
cellulose: DO, drug dose  
decanoic acid: CM, drug comparison  
decanoic acid: DO, drug dose  
decanoic acid: CB, drug combination  
lauric acid: CB, drug combination  
lauric acid: CM, drug comparison  
myristic acid: CB, drug combination  
myristic acid: CM, drug comparison  
saturated fatty acid: DO, drug dose  
saturated fatty acid: CM, drug comparison  
saturated fatty acid: CB, drug combination

CAS REGISTRY NO.: (captopril) 62571-86-2; (cellulose) 61991-22-8, 68073-05-2, 9004-34-6; (decanoic acid) 334-48-5, 3398-75-2; (lauric acid) 115-05-9, 143-07-7; (myristic acid) 1715-79-3, 544-63-8

COMPANY NAME: Sigma (United States); Tci (Japan); Teh sheng (Taiwan, Province of China)

L264 ANSWER 47 OF 63 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 95030215 EMBASE  
 DOCUMENT NUMBER: 1995030215  
 TITLE: Application of peptide-based **matrix** metalloproteinase inhibitors in corneal ulceration.  
 AUTHOR: Gray R.D.; Paterson C.A.  
 CORPORATE SOURCE: Department of Biochemistry, Univ Louisville School of Medicine, Louisville, KY 40292, United States  
 SOURCE: Annals of the New York Academy of Sciences, (1994) Vol. 732, pp. 206-216. .  
 ISSN: 0077-8923 CODEN: ANYAA  
 COUNTRY: United States  
 DOCUMENT TYPE: Journal; Conference Article  
 FILE SEGMENT: 005 General Pathology and Pathological Anatomy  
 012 Ophthalmology  
 029 Clinical Biochemistry  
 030 Pharmacology  
 037 Drug Literature Index  
 LANGUAGE: English  
 ENTRY DATE: Entered STN: 15 Feb 1995  
 Last Updated on STN: 15 Feb 1995  
 CONTROLLED TERM: Medical Descriptors:  
 \*cornea ulcer  
 animal experiment  
 animal model  
 caustic burn  
 conference paper  
 controlled study  
 cornea  
 cornea injury  
 cornea perforation  
 drug structure  
 eye infection  
 keratitis  
 nonhuman  
 pseudomonas aeruginosa  
 rabbit  
**topical drug administration**  
 wound healing  
 Drug Descriptors:  
 collagen  
 \*metalloproteinase inhibitor: AN, drug analysis  
 \*metalloproteinase inhibitor: DV, drug development  
**captopril**  
 collagenase: EC, endogenous compound  
 gelatinase: EC, endogenous compound  
 metalloproteinase: EC, endogenous compound  
 CAS REGISTRY NO.: (collagen) 9007-34-5; (captopril) 62571-86-2; (collagenase) 9001-12-1; (gelatinase) 9040-48-6; (metalloproteinase) 81669-70-7

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ACCESSION NUMBER: 94096790 EMBASE  
DOCUMENT NUMBER: 1994096790  
TITLE: The USA experience with the clonidine transdermal  
therapeutic system.  
AUTHOR: Burris J.F.  
CORPORATE SOURCE: Depts of Medicine and Pharmacology, NE 120, Georgetown  
University Medical Center, 3900 Reservoir Road  
NW, Washington, DC, United States  
SOURCE: Clinical Autonomic Research, (1993) Vol. 3, No. 6, pp.  
391-396. .  
ISSN: 0959-9851 CODEN: CAURE  
COUNTRY: United Kingdom  
DOCUMENT TYPE: Journal; Conference Article  
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery  
030 Pharmacology  
037 Drug Literature Index  
038 Adverse Reactions Titles  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ENTRY DATE: Entered STN: 14 Apr 1994  
Last Updated on STN: 14 Apr 1994

ABSTRACT: Cardiovascular diseases are the leading causes of death in the United States, with hypertension being amongst the most prevalent of the cardiovascular risk factors. Improvement of hypertension management has, in consequence, received much attention. Extensive pre- and post-marketing experience with the transdermal formulation of clonidine marketed in the USA in the mid-1980s has now been accumulated. Transdermal clonidine is effective as monotherapy in mild-moderate hypertension, and in combination with diuretics, calcium antagonists and ACE inhibitors in more resistant cases. It controls blood pressure throughout the 24-h circadian cycle. It is effective and generally well-tolerated in adolescents, the elderly, blacks, diabetics, and subjects with chronic renal insufficiency. It has been used perioperatively and for suppression of adrenergic symptoms in subjects withdrawing from addicting substances. In comparison with oral clonidine, transdermal clonidine reduces the incidence and severity of such symptomatic side-effects as dry mouth, drowsiness, and sexual dysfunction. Minor skin reactions occur at the site of application of the transdermal patch with moderate frequency. Adherence to transdermal clonidine therapy is high, and patients commonly prefer it to oral therapy. Transdermal administration of clonidine is a useful therapeutic advance in the long-term management of hypertension.

CONTROLLED TERM: Medical Descriptors:  
\*hypertension: DT, drug therapy  
\*transdermal drug administration  
blood pressure regulation  
cardiovascular disease  
circadian rhythm  
clinical trial  
conference paper  
controlled study  
drowsiness: SI, side effect  
drug efficacy  
drug tolerance  
human  
major clinical study  
multicenter study  
oral drug administration  
patient compliance  
sexual dysfunction: SI, side effect

skin manifestation: SI, side effect  
xerostomia: SI, side effect  
Drug Descriptors:  
\*clonidine: AE, adverse drug reaction  
\*clonidine: CT, clinical trial  
\*clonidine: DT, drug therapy  
\*clonidine: CM, drug comparison  
\*clonidine: CB, drug combination  
\*clonidine: AD, drug administration  
antihypertensive agent: CT, clinical trial  
antihypertensive agent: AD, drug administration  
antihypertensive agent: DT, drug therapy  
antihypertensive agent: CM, drug comparison  
antihypertensive agent: CB, drug combination  
antihypertensive agent: AE, adverse drug reaction  
calcium channel blocking agent: DT, drug therapy  
calcium channel blocking agent: CB, drug combination  
  captopril: CM, drug comparison  
diltiazem: CB, drug combination  
diltiazem: DT, drug therapy  
  dipeptidyl carboxypeptidase inhibitor: CB, drug  
  combination  
  dipeptidyl carboxypeptidase inhibitor: DT, drug  
  therapy  
diuretic agent: DT, drug therapy  
diuretic agent: CB, drug combination  
  enalapril: CB, drug combination  
  enalapril: DT, drug therapy  
CAS REGISTRY NO.: (clonidine) 4205-90-7, 4205-91-8, 57066-25-8; (captopril)  
62571-86-2; (diltiazem) 33286-22-5, 42399-41-7; (enalapril)  
75847-73-3

L264 ANSWER 49 OF 63 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights  
reserved on STN  
ACCESSION NUMBER: 92293015 EMBASE  
DOCUMENT NUMBER: 1992293015  
TITLE: Issues in contemporary drug delivery. Part VI: Advanced  
cardiac drug formulations.  
AUTHOR: Hilleman D.E.; Banakar U.V.  
CORPORATE SOURCE: St. Louis College of Pharmacy, 4588 Parkview Place, St.  
Louis, MO 63110, United States  
SOURCE: Journal of Pharmacy Technology, (1992) Vol. 8, No. 5, pp.  
203-211.  
ISSN: 8755-1255 CODEN: JPTEEB  
COUNTRY: United States  
DOCUMENT TYPE: Journal; General Review  
FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery  
027 Biophysics, Bioengineering and Medical  
Instrumentation  
030 Pharmacology  
037 Drug Literature Index  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ENTRY DATE: Entered STN: 25 Oct 1992  
Last Updated on STN: 25 Oct 1992  
ABSTRACT: Objective: To identify and discuss the clinical utility of new  
delivery systems and formulations of cardiac drugs. Data Sources: Studies  
describing or evaluating new drug delivery systems for cardiac drugs were  
identified through a MEDLINE literature search. Study Selection: All studies  
describing or evaluating new delivery systems for cardiac drugs were reviewed.

Data Extraction: Data were abstracted and evaluated by each author independently. Data Synthesis: The most common oral sustained-release formulations include the wax-matrix system, the gastrointestinal therapeutic system (GITS), and the spheroidal oral drug absorption system (SODAS). The wax-matrix delivery system is limited by the occurrence of 'dose-dumping.' In a low-pH setting, the wax-matrix formulation may dissolve too rapidly, liberating the entire dose in a short period of time. The clinical relevance of this phenomenon is unknown. The GITS and SODAS formulations are less likely to be affected by pH and food. Nitroglycerin is available by many routes of administration. The topical patch forms are convenient to use, but are associated with the development of tolerance. A buccal formulation incorporates a relatively short onset of effect with a three- or four-times-daily dosing regimen. Although tolerance is less of a problem with buccal nitroglycerin than with topical nitrates, this formulation is less convenient to use because of buccal irritation and interference with eating and talking. A new spray formulation of nitroglycerin offers longer shelf-life storage stability and an easier mode of administration. The spray canister is stable for three years compared with 12 weeks for an opened bottle of sublingual nitroglycerin tablets. Sublingual administration of oral cardiac drugs offers the potential for a more rapid onset of effects. Although nifedipine is often given sublingually, objective data indicate that it is not absorbed buccally but rather in the stomach. It appears that the chew-and-swallow route is most appropriate for nifedipine. Captopril is absorbed sublingually but its efficacy has not been demonstrated. Transdermal clonidine improves compliance and is associated with fewer adverse effects than oral clonidine. Transdermal formulations of beta-blockers are currently being evaluated. Conclusions: Further advancements in the development of novel delivery systems for cardiac drugs are expected in the future.

CONTROLLED TERM: Medical Descriptors:  
 \*cardiovascular disease  
 \*data analysis  
 angina pectoris  
 drug formulation  
 drug information  
 drug release  
 drug research  
 human  
 hyperlipoproteinemia  
 hypertension  
 oral drug administration  
 review  
 sublingual drug administration  
     **topical drug administration**  
     **transdermal drug administration**  
 drug delivery system  
 sustained release preparation  
 Drug Descriptors:  
 \*cardiovascular agent: CR, drug concentration  
 \*cardiovascular agent: PR, pharmaceuticals  
 \*cardiovascular agent: PK, pharmacokinetics  
     **captopril: PK, pharmacokinetics**  
     **captopril: CR, drug concentration**  
     **captopril: PR, pharmaceuticals**  
 clonidine: CR, drug concentration  
 clonidine: PR, pharmaceuticals  
 clonidine: PK, pharmacokinetics  
 colestyramine: PR, pharmaceuticals  
 colestyramine: CR, drug concentration  
 colestyramine: PK, pharmacokinetics

diltiazem: PD, pharmacology  
 diltiazem: PK, pharmacokinetics  
 diltiazem: PR, pharmaceutics  
 metoprolol: PK, pharmacokinetics  
 metoprolol: CR, drug concentration  
 metoprolol: PR, pharmaceutics  
 nifedipine: CR, drug concentration  
 nifedipine: PK, pharmacokinetics  
 nifedipine: PR, pharmaceutics  
 procainamide: CR, drug concentration  
 procainamide: PR, pharmaceutics  
 procainamide: PK, pharmacokinetics  
 propranolol: PR, pharmaceutics  
 propranolol: PK, pharmacokinetics  
 propranolol: CR, drug concentration  
 timolol: CR, drug concentration  
 timolol: PR, pharmaceutics  
 timolol: PK, pharmacokinetics  
 verapamil: PK, pharmacokinetics  
 verapamil: PR, pharmaceutics  
 verapamil: CR, drug concentration

CAS REGISTRY NO.: (captopril) 62571-86-2; (clonidine) 4205-90-7, 4205-91-8, 57066-25-8; (colestyramine) 11041-12-6, 58391-37-0; (diltiazem) 33286-22-5, 42399-41-7; (metoprolol) 37350-58-6; (nifedipine) 21829-25-4; (procainamide) 51-06-9, 614-39-1; (propranolol) 13013-17-7, 318-98-9, 3506-09-0, 4199-09-1, 525-66-6; (timolol) 26839-75-8; (verapamil) 152-11-4, 52-53-9

CHEMICAL NAME: Cardizem; Calan; Isoptin; Verelan; Inderal la; Procan sr; Pronestyl sr; Cholybar

L264 ANSWER 50 OF 63 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:454319 BIOSIS

DOCUMENT NUMBER: PREV200400459228

TITLE: **Transdermal administration of ACE inhibitors.**

AUTHOR(S): Li, Chensheng [Inventor, Reprint Author]; Nguyen, Viet [Inventor]

CORPORATE SOURCE: Miami, FL, USA

ASSIGNEE: Noven Pharmaceuticals, Inc.

PATENT INFORMATION: US 6805878 20041019

SOURCE: Official Gazette of the United States Patent and Trademark Office Patents, (Oct 19 2004) Vol. 1287, No. 3.  
<http://www.uspto.gov/web/menu/patdata.html>. e-file.  
 ISSN: 0098-1133 (ISSN print).

DOCUMENT TYPE: Patent

LANGUAGE: English

ENTRY DATE: Entered STN: 24 Nov 2004

Last Updated on STN: 24 Nov 2004

ABSTRACT: Disclosed is a dermal composition comprising enalapril ethyl ester or another prodrug corresponding to a pharmaceutically active form of an \*\*\*ACE\*\*\* inhibitor in an amount corresponding to a therapeutically effective amount of enalaprilat (or other pharmaceutically active form of enalapri) or pharmaceutically active form of the ACE \*\*\*inhibitor\*\*\* in admixture with a pharmaceutically acceptable carrier. In a preferred embodiment, the carrier is a pressure-sensitive adhesive matrix comprising a polymer or polymer blend. The dermal composition is applied in a method of substantially increasing the flux of enalaprilat through the skin of a human or an animal by maintaining the dermal composition in contact with the

skin.

NAT. PATENT. CLASSIF.:424449000

CONCEPT CODE: Biochemistry studies - Proteins, peptides and amino acids  
10064  
Pathology - Therapy 12512  
Integumentary system - Pathology 18506  
Pharmacology - General 22002  
Pharmacology - Clinical pharmacology 22005  
Pharmacology - Integumentary system, dental and oral  
biology 22020

INDEX TERMS: Major Concepts  
Dermatology (Human Medicine, Medical Sciences);  
Pharmacology

INDEX TERMS: Chemicals & Biochemicals  
enalaprilat [ACE inhibitor]:  
dermatological-drug

ORGANISM: Classifier  
Animalia 33000  
Super Taxa  
Animalia  
Organism Name  
animal (common)  
Taxa Notes  
Animals

ORGANISM: Classifier  
Hominidae 86215  
Super Taxa  
Primates; Mammalia; Vertebrata; Chordata; Animalia  
Organism Name  
human (common)  
Taxa Notes  
Animals, Chordates, Humans, Mammals, Primates,  
Vertebrates

REGISTRY NUMBER: 76420-72-9 (enalaprilat)  
76420-72-9 (ACE inhibitor)

L264 ANSWER 51 OF 63 DRUGU COPYRIGHT 2006 THE THOMSON CORP on STN

ACCESSION NUMBER: 1993-17563 DRUGU T S

TITLE: Effect of Captopril in Nitrate Tolerance.

AUTHOR: Bussmann W D; Felsinger K

LOCATION: Frankfurt, Germany, West

SOURCE: Dtsch.Med.Wochenschr. (118, No. 7, 209-12, 1993) 4 Fig. 11  
Ref.

CODEN: DMWOAX ISSN: 0012-0472

AVAIL. OF DOC.: Abteilung fuer Kardiologie, Zentrum der Inneren Medizin,  
Klinikum der Universitaet, Theodor-Stern-Kai 7, W-6000  
Frankfurt/Main 70, Germany.

LANGUAGE: German

DOCUMENT TYPE: Journal

#### ABSTRACT:

Captopril p.o. induced an antiischemic effect measured by exercise ECG in 17 men with coronary artery stenosis. The effect was less than that achieved after acute application of a nitrate **plaster**, but the two treatments showed synergistic effects when given together. After development of nitrate tolerance through continuous application of **plasters**, captopril restored both the ECG and subjective antiischemic effects to nearly all those observed after acute nitrate application. Nitrate headache caused the premature withdrawal of 2 subjects. Neither B.P. nor HR were affected by nitrate and/or

captopril.

SECTION HEADING: T Therapeutics  
S Adverse Effects

CLASSIF. CODE: 35 Adverse Reactions  
56 Cardiants  
66 Drug Interactions

CONTROLLED TERM:

ANGINA-PECTORIS \*TR; CARDIOPATHY \*TR; CORONARY-DISEASE \*TR;  
IN-VIVO \*FT; CASES \*FT; ELECTROCARDIOGRAPHY \*FT; SYNERGIST  
\*FT; BLOOD-PRESSURE \*FT; HEART-RATE \*FT; EXERCISE \*FT;  
HEMODYNAMICS \*FT

[01] CAPTOPRIL \*TR; CAPTOPRIL \*DI; P.O. \*FT; CARDIANT \*FT;  
**ACE-INHIBITOR** \*FT; HYPOTENSIVES \*FT;  
ANGIOTENSIN-ANTAGONISTS \*FT; CAPTOPRIL \*RN; TR \*FT; DI \*FT

CAS REGISTRY NO.: 62571-86-2

[02] HEADACHE \*AE; CAPTOPRIL \*DI; **PLASTER** \*FT;  
PHARM.PREP. \*FT; TOLERANCE \*FT; CARDIOGLYCOSIDES \*FT;  
**PATCH** \*FT; CARDIOGLYCOSIDE \*FT; TRANSDERMAL \*FT;  
CARDIANTS \*FT; CARDIANT \*FT; TR \*FT; DI \*FT; AE \*FT

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

L264 ANSWER 52 OF 63 DRUGU COPYRIGHT 2006 THE THOMSON CORP on STN

ACCESSION NUMBER: 1992-50978 DRUGU T

TITLE: Effect of Captopril on Pre-existent Nitrate Tolerance.

AUTHOR: Bussmann W D; Felsing K

LOCATION: Frankfurt, Germany, West

SOURCE: Z.Kardiol. (81, Suppl. 3, 19, 1992)

CODEN: ZKRDAX ISSN: 0300-5860

AVAIL. OF DOC.: Abtlg. Kardiologie, Zentrum Innere Medizin, Klinikum der  
Universitaet, Frankfurt, Germany.

LANGUAGE: German

DOCUMENT TYPE: Journal

ABSTRACT:

Continuous treatment with glycerol trinitrate (GTN) **plasters**, and also with captopril (with and without GTN) was studied in 15 patients with coronary heart disease (CHD). During GTN treatment the decrease in ST-wave depression lessened with the development of nitrate tolerance. ST-depression was decreased more with captopril during nitrate tolerance than with captopril alone. Authors conclude that the anti-ischemic effects of GTN (during nitrate tolerance) and captopril appear to be additive. (congress abstract).

SECTION HEADING: T Therapeutics

CLASSIF. CODE: 56 Cardiants

CONTROLLED TERM:

ANGINA-PECTORIS \*TR; CARDIOPATHY \*TR; CORONARY-DISEASE \*TR;  
CASES \*FT; IN-VIVO \*FT; ADDITIVE \*FT; EXERCISE \*FT; ALONE  
\*FT; COMB. \*FT; CARDIANT \*FT

[01] NITROGLYCEROL \*TR; TOLERANCE \*FT; **PATCH** \*FT;  
TRANSDERMAL \*FT; CARDIANTS \*FT; SPASMOLYTICS \*FT;  
CALCIUM-ANTAGONISTS \*FT; NITROGLYC \*RN; TR \*FT

CAS REGISTRY NO.: 55-63-0

[02] CAPTOPRIL \*TR; **ACE-INHIBITOR** \*FT;

HYPOTENSIVES \*FT; ANGIOTENSIN-ANTAGONISTS \*FT; CAPTOPRIL \*RN;  
TR \*FT

CAS REGISTRY NO.: 62571-86-2  
FIELD AVAIL.: AB; LA; CT  
FILE SEGMENT: Literature

L264 ANSWER 53 OF 63 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN

ACCESSION NUMBER: 2005-132608 [14] WPIX

CROSS REFERENCE: 2005-682785 [70]

DOC. NO. CPI: C2005-043759

TITLE: New pharmaceutical composition for preventing and/or  
treating cardiovascular, cerebrovascular and peripheral  
vascular diseases, containing vitamin D receptor  
activators (VDRA) or Vitamin D analogs.

DERWENT CLASS: B05 D16 P62

INVENTOR(S): JONES, T M; LEHNERT, M W; SCHIAPPACASSE, J M; MELNICK, J  
Z; OSTROW, D H; SUN, E; TIAN, J; TONER, E S; WILLIAMS, L  
A; WU-WONG, J R; DELGADO-HERRERA, L; FISHER, C J;  
MELNICK, J; OSTROW, D; TONER, S; WILLIAMS, L

PATENT ASSIGNEE(S): (JONE-I) JONES T M; (LEHN-I) LEHNERT M W; (SCHI-I)  
SCHIAPPACASSE J M; (MELN-I) MELNICK J Z; (OSTR-I) OSTROW  
D H; (SUNE-I) SUN E; (TIAN-I) TIAN J; (TONE-I) TONER E S;  
(WILL-I) WILLIAMS L A; (WUWO-I) WU-WONG J R; (ABBO)  
ABBOTT LAB

COUNTRY COUNT: 108

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN	IPC
WO 2005011651	A2	20050210	(200514)*	EN	26	A61K031-00	
RW:	AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE						
	LS LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW						
W:	AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE						
	DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG						
	KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ						
	OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG						
	US UZ VC VN YU ZA ZM ZW						
US 2005092143	A1	20050505	(200531)			B25B023-151	
US 2005192255	A1	20050901	(200558)			A61K031-59	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2005011651	A2	WO 2004-US23952	20040730
US 2005092143	A1 Provisional	US 2003-491088P	20030730
		US 2004-903577	20040730
US 2005192255	A1 Provisional	US 2003-491088P	20030730
		US 2004-903039	20040729

PRIORITY APPLN. INFO: US 2003-491088P 20030730; US  
2004-903577 20040730; US  
2004-903039 20040729

INT. PATENT CLASSIF.:

MAIN: A61K031-00; A61K031-59; B25B023-151

SECONDARY: A61K009-70

BASIC ABSTRACT:

WO2005011651 A UPAB: 20051101

NOVELTY - A sustained release pharmaceutical composition for preventing,

treating and delaying progression of cardiovascular, cerebrovascular and peripheral vascular diseases, comprising vitamin D receptor activators (VDRA) or Vitamin D analogs, and optionally at least one an angiotensin converting enzyme inhibitor, an angiotensin (II) receptor (I) blocker, and an aldosterone blocker, is new.

DETAILED DESCRIPTION - The cardiovascular, cerebrovascular and peripheral vascular diseases prevented or delayed by the pharmaceutical composition cited above includes heart failure, cardiomyopathy, atherosclerosis, myocardial infarction, and cerebrovascular accident.

INDEPENDENT CLAIMS are also included for the following:

(1) a pharmaceutical composition for treating, preventing or delaying progression of vascular disease in a mammal, comprising a Vitamin D receptor activator or Vitamin D analog, and optionally at least one angiotensin converting enzyme inhibitor, an angiotensin (II) receptor (I) blocker, and an aldosterone blocker;

(2) a method of preventing, treating and delaying disease progression of vascular disease in a mammal, comprising administering to the mammal a pharmaceutical composition of (1); and

(3) a method of treating, inhibiting or preventing vascular disease in a mammal by reducing PAI-1 expression in the mammal, comprising administering to the mammal a VDRA or Vitamin D analog.

ACTIVITY - Cardiovascular-Gen.; Cardiant; Cerebroprotective; Vasotropic; Antiarteriosclerotic. Experimentally induced vitamin D deficiency was associated with cardiac hypertrophy and hypertension in normal adult Sprague-Dawley rats. Vitamin D was shown to inhibit endothelin-induced hypertrophy of neonatal rat cardiac myocytes in culture. This was associated with a reduction in expression of the ANP, BNP and alpha skeletal actin genes and suppression of the human ANP and BNP gene promoters.

MECHANISM OF ACTION - Vitamin-D.

USE - The pharmaceutical composition is useful in preventing, treating and delaying disease progression of cardiovascular, cerebrovascular and peripheral vascular diseases, such as heart failure, cardiomyopathy, atherosclerosis, myocardial infarction, and cerebrovascular accident.

Dwg.0/12

FILE SEGMENT: CPI GMPI  
 FIELD AVAILABILITY: AB; DCN  
 MANUAL CODES: CPI: B03-G; B04-E01; B04-M01; B10-E04A; B11-C04A;  
 B12-M02D; B12-M02F; B12-M07;  
 B12-M10A; B12-M12C; B12-M12K; B12-M12N; B14-D02A1;  
 B14-D03; B14-F01; B14-F02B; B14-F02B1;  
 B14-J01; B14-N16; D05-A02; D05-H01

L264 ANSWER 54 OF 63 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN  
 ACCESSION NUMBER: 2005-217828 [23] WPIX  
 DOC. NO. CPI: C2005-069810  
 TITLE: Percutaneous absorption adhesive patch contains base containing adhesive layer and support, where adhesive layer contains an enalapril analog.  
 DERWENT CLASS: A96 B03 B07 D22  
 PATENT ASSIGNEE(S): (NITL) NITTO DENKO CORP  
 COUNTRY COUNT: 1  
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN	IPC
JP 2005060291	A	20050310	(200523)*		10	A61K038-00	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
JP 2005060291	A	JP 2003-291796	20030811

PRIORITY APPLN. INFO: JP 2003-291796 20030811  
 INT. PATENT CLASSIF.:

MAIN: A61K038-00

SECONDARY: A61K009-70; A61K047-14; A61K047-32

# BASIC ABSTRACT:

JP2005060291 A UPAB: 20050411

NOVELTY - A percutaneous absorption adhesive patch contains a base containing an adhesive layer and a support. The adhesive layer contains an enalapril analog (I) and is an adhesive layer having a surface pH of more than 7 or a rubber-based adhesive layer.

DETAILED DESCRIPTION - A percutaneous absorption adhesive patch contains a base containing an adhesive layer and a support. The adhesive layer contains an enalapril analog (I) and is an adhesive layer having a surface pH of more than 7 or a rubber-based adhesive layer.

R = 2-8C alkyl.

ACTIVITY - Hypotensive.

No suitable test details are given.

MECHANISM OF ACTION - ACE-Inhibitor.

No suitable test details are given.

USE - Used as a transdermal preparation having base containing prodrug of enalapril, which is angiotensin-converting enzyme inhibitor used as antihypertensive.

ADVANTAGE - By using the adhesive or rubber-based adhesive agent having a surface pH of more than 7, as a base containing the enalapril analog, an adhesive patch having favorable percutaneous absorbability and storage stability is obtained. Enalapril formulated as percutaneous absorption adhesive patch produces few side effects. The adhesive layer having surface pH of more than 7 avoids skin irritation.

Dwg.0/0

FILE SEGMENT: CPI

FIELD AVAILABILITY: AB; GI; DCN

MANUAL CODES: CPI: A12-V01; A12-V03A; B04-C03B; B04-C03D; B07-D03;  
 B10-G02; B12-M02D; B12-M02F;  
 B14-F02B; B14-F02B1; D09-C04B

L264 ANSWER 55 OF 63. WPIX COPYRIGHT 2006 THE THOMSON CORP on STN

ACCESSION NUMBER: 2004-766334 [75] WPIX

DOC. NO. NON-CPI: N2004-604629

DOC. NO. CPI: C2004-268663

TITLE: Electrotransport device for e.g. transdermal delivery of therapeutic agent comprises two reservoirs connected to two electrodes, power source, electronic circuitry connected to electrode, and reservoir housing.

DERWENT CLASS: B05 B07 P34 S05

INVENTOR(S): GYORY, J R; GYORY, R J

PATENT ASSIGNEE(S): (GYOR-I) GYORY J R; (ALZA) ALZA CORP

COUNTRY COUNT: 109

# PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN	IPC
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WO 2004089464	A1	20041021	(200475)*	EN	20	A61N001-30	
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RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE  
 LS LU MC MW MZ NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE  
 DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG  
 KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NI NO NZ  
 OM PG PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG  
 US UZ VC VN YU ZA ZM ZW  
 US 2005004506 A1 20050106 (200504) A61N001-30  
 AU 2004227851 A1 20041021 (200568) A61N001-30  
 NO 2005004946 A 20051025 (200578) A61N001-30  
 EP 1608433 A1 20051228 (200603) EN A61N001-30  
 R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV  
 MC MK NL PL PT RO SE SI SK TR  
 MX 2005010497 A1 20051101 (200625) A61N001-30

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2004089464	A1	WO 2004-US9831	20040330
US 2005004506	A1 Provisional	US 2003-459539P	20030331
		US 2004-814705	20040330
AU 2004227851	A1	AU 2004-227851	20040330
NO 2005004946	A	NO 2005-4946	20051025
EP 1608433	A1	EP 2004-758646	20040330
		WO 2004-US9831	20040330
MX 2005010497	A1	WO 2004-US9831	20040330
		MX 2005-10497	20050929

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2004227851	A1 Based on	WO 2004089464
EP 1608433	A1 Based on	WO 2004089464
MX 2005010497	A1 Based on	WO 2004089464

PRIORITY APPLN. INFO: US 2003-459539P 20030331; US  
 2004-814705 20040330

## INT. PATENT CLASSIF.:

MAIN: A61N001-30

## BASIC ABSTRACT:

WO2004089464 A UPAB: 20041122

NOVELTY - An electrotransport device comprises two reservoirs connected to two electrodes respectively, a power source, an electronic circuitry connected to at least one electrode, and a reservoir housing.

DETAILED DESCRIPTION - An electrotransport device comprises two reservoirs (R1 and R2) connected to two electrodes respectively; a power source; electronic circuitry connected to at least one electrode; and a reservoir housing (H1). (R1) And (R2) receive an active agent formulation and an electrolyte formulation respectively. (H1) Has an internal cavity to receive (R1) and associated electrode; and includes an integral conductive element having a first end connected to (R1) and a second end disposed on the outside of (H1) and extends from it. The second end of the conductive element is operatively connected to the power source, so that there is electrical connection between (R1), the electronic circuitry and the power source.

USE - As transdermal therapeutic agent delivery and sampling device.

ADVANTAGE - There is tight liquid and moisture bond formed between the material forming the reservoir housing and the conductive element; and also the reservoir housing is a single integral component that does not require the fabrication of openings or other passages, hence the problem

of water and/or moisture leakage from the reservoir housing is eliminated.  
Dwg.0/4

FILE SEGMENT: CPI EPI GMPI  
FIELD AVAILABILITY: AB; DCN  
MANUAL CODES: CPI: B04-A01; B04-A04; B04-C01; B04-H03; B04-J04B;  
B04-N04; B06-D13; B07-A01; B07-B01; B07-D05;  
B10-B02F; B10-B03B; B11-C08C; B12-K04;  
B12-M02F; B14-C01; B14-E05; B14-F02B;  
B14-F02B1; B14-J02C  
EPI: S05-A04A; S05-J02

L264 ANSWER 56 OF 63 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN  
ACCESSION NUMBER: 2003-402862 [38] WPIX  
DOC. NO. CPI: C2003-107124  
TITLE: Transdermal administration of enalaprilat involves application of a dermal composition comprising an enalapril ester and maintaining the composition in contact with skin.

DERWENT CLASS: A96 B03 D22  
INVENTOR(S): LI, C; NGUYEN, V  
PATENT ASSIGNEE(S): (LICC-I) LI C; (NGUY-I) NGUYEN V; (NOVE-N) NOVEN PHARM INC  
COUNTRY COUNT: 101  
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN	IPC
WO 2003022270	A1	20030320	(200338)*	EN	18	A61K031-40	
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SK SL SZ TR TZ UG ZM ZW							
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW							
US 2003064933	A1	20030403	(200338)			A61K038-05	
BR 2002012506	A	20040824	(200458)			A61K031-40	
AU 2002332544	A1	20030324	(200461)			A61K031-40	
KR 2004044907	A	20040531	(200463)			A61K031-401	
US 6805878	B2	20041019	(200469)			A61F013-00	
JP 2005502689	W	20050127	(200510)		51	A61K031-401	
US 2005100589	A1	20050512	(200532)			A61K031-401	

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003022270	A1	WO 2002-US25981	20020913
US 2003064933	A1 Provisional	US 2001-318632P	20010913
		US 2001-14785	20011214
BR 2002012506	A	BR 2002-12506	20020913
		WO 2002-US25981	20020913
AU 2002332544	A1	AU 2002-332544	20020913
KR 2004044907	A	KR 2004-703693	20040312
US 6805878	B2 Provisional	US 2001-318632P	20010913
		US 2001-14785	20011214
JP 2005502689	W	WO 2002-US25981	20020913
		JP 2003-526399	20020913
US 2005100589	A1 Provisional	US 2001-318632P	20010913
	Cont of	US 2001-14785	20011214

US 2004-965226

20041015

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
BR 2002012506	A Based on	WO 2003022270
AU 2002332544	A1 Based on	WO 2003022270
JP 2005502689	W Based on	WO 2003022270
US 2005100589	A1 Cont of	US 6805878

PRIORITY APPLN. INFO: US 2001-14785 20011214; US  
 2001-318632P 20010913; US  
 2004-965226 20041015

## INT. PATENT CLASSIF.:

MAIN: A61F013-00; A61K031-40; A61K031-401; A61K038-05  
 SECONDARY: A61F013-02; A61K009-70; A61K047-10; A61K047-30;  
 A61K047-32; A61K047-34; A61L015-16; A61P009-04;  
 A61P009-10; A61P009-12; A61P013-12; A61P043-00

## BASIC ABSTRACT:

WO2003022270 A UPAB: 20030616

NOVELTY - Transdermal administration of enalaprilat involves applying a dermal composition comprising an enalapril ester along with a carrier and maintaining the composition in contact with the skin. The flux of enalapril ester is greater than that of enalapril maleate.

ACTIVITY - Hypotensive; Cardiant; Nephrotropic.

MECHANISM OF ACTION - Angiotensin-Converting Enzyme (ACE) Inhibitor.

USE - For transdermally administering enalapril/enalaprilat through the skin; and for treating ACE inhibiting conditions e.g. hypertension, heart failure, myocardial infarction and nephropathy (all claimed).

ADVANTAGE - The method substantially increases the flux of enalapril/enalaprilat through the skin.

Dwg.0/2

FILE SEGMENT: CPI  
 FIELD AVAILABILITY: AB; DCN  
 MANUAL CODES: CPI: A12-V01; A12-V03A; B04-C03; B07-D03; B10-E04C;  
 B10-E04D; **B12-M02F**; B14-F01;  
**B14-F02B1**; B14-N10; D09-C04B

L264 ANSWER 57 OF 63 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN  
 ACCESSION NUMBER: 2000-558257 [51] WPIX  
 DOC. NO. CPI: C2000-166236  
 TITLE: Percutaneous absorption preparations comprise an angiotensin II receptor antagonist and percutaneous absorption promoter.

DERWENT CLASS: A96 B02  
 INVENTOR(S): IGA, K; NAKA, T; SUZUKI, Y  
 PATENT ASSIGNEE(S): (TAKE) TAKEDA CHEM IND LTD  
 COUNTRY COUNT: 90  
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN	IPC
WO 2000048634	A1	20000824	(200051)*	JA	57	A61K045-00	
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL							
OA PT SD SE SL SZ TZ UG ZW							
W: AE AL AM AU AZ BA BB BG BR BY CA CN CR CU CZ DM EE GD GE HR HU ID							
IL IN IS JP KG KR KZ LC LK LR LT LV MA MD MG MK MN MX NO NZ PL RO							
RU SG SI SK SL TJ TM TR TT TZ UA US UZ VN YU ZA							
JP 2000302695	A	20001031	(200059)		22	A61K045-08	

AU 2000025738 A 20000904 (200103) A61K045-00  
 EP 1153613 A1 20011114 (200175) EN A61K045-00  
 R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT  
 RO SE SI  
 JP 2000599424 X 20020604 (200239) A61K045-00

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000048634	A1	WO 2000-JP926	20000218
JP 2000302695	A	JP 2000-46819	20000218
AU 2000025738	A	AU 2000-25738	20000218
EP 1153613	A1	EP 2000-904029	20000218
		WO 2000-JP926	20000218
JP 2000599424	X	JP 2000-599424	20000218
		WO 2000-JP926	20000218

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2000025738	A Based on	WO 2000048634
EP 1153613	A1 Based on	WO 2000048634
JP 2000599424	X Based on	WO 2000048634

PRIORITY APPLN. INFO: JP 1999-42396 19990219

## INT. PATENT CLASSIF.:

MAIN: A61K045-00; A61K045-08  
 SECONDARY: A61K009-70; A61K031-4178; A61K031-4184; A61K031-4245;  
 A61K047-10; A61K047-14; A61K047-16; A61K047-34;  
 A61P009-12; A61P043-00  
 ADDITIONAL: C07D403-10; C07D413-10  
 INDEX: C07D403-10, C07D413:10

## BASIC ABSTRACT:

WO 200048634 A UPAB: 20001016

NOVELTY - Percutaneous absorption preparations comprise an angiotensin II receptor antagonist and a percutaneous absorption promoter.

DETAILED DESCRIPTION - Percutaneous absorption preparations comprise an angiotensin II receptor antagonist and a percutaneous absorption promoter.

An INDEPENDENT CLAIM is also included for a percutaneous absorption preparations comprising an angiotensin II receptor antagonist and a fatty acid ester, a polyol or a nonionic surfactant.

ACTIVITY - Hypotensive; cardiant; cerebroprotective; vasotropic; antidiabetic; ophthalmological; nephrotropic; antiarteriosclerotic; endocrine; antilipemic; antianginal; thrombolytic; anticoagulant; central nervous system active; nootropic; neuroprotective; antidepressant.

MECHANISM OF ACTION - Angiotensin antagonist II.

USE - The percutaneous absorption preparations are useful for administering angiotensin II receptor antagonists which are useful for the treatment and prevention of e.g. hypertension, fatty heart, cardiovascular infarction, cerebral apoplexy, peripheral circulatory ischemic disorders, diabetes, diabetic retinopathy, nephritis, arteriosclerosis, cardiovascular occlusion, hyperaldosterone, kidney failure, cataracts, hyperlipidemia, angina, thrombosis, central nervous disorders, Alzheimer's disease, depression, senile dementia and multiple organ failure.

ADVANTAGE - The percutaneous absorption preparations give the correct skin permeation rate over a long period.

Dwg.0/0

FILE SEGMENT: CPI  
 FIELD AVAILABILITY: AB; DCN  
 MANUAL CODES: CPI: A12-V01; B06-D05; **B12-M02D**; B14-F01;  
**B14-F02B1**; B14-F06; B14-F07; B14-J01A1;  
 B14-J01A4; B14-N03; B14-N10; B14-N16; B14-S04

L264 ANSWER 58 OF 63 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN  
 ACCESSION NUMBER: 1993-386170 [48] WPIX  
 DOC. NO. CPI: C1993-171667  
 TITLE: Transdermal drug, especially captopril, delivery system - with  
 drug reservoir containing aliphatic ester and alcohol as  
 synergistic drug permeation enhancer.  
 DERWENT CLASS: A96 B03 B07  
 INVENTOR(S): CATZ, P G; FRIEND, D R; NOLEN, H W  
 PATENT ASSIGNEE(S): (STRI) SRI INT  
 COUNTRY COUNT: 19  
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN	IPC
WO 9323019	A1	19931125	(199348)*	EN	31	A61K009-70	
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE							
W: CA JP KR							

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9323019	A1	WO 1993-US4442	19930510

PRIORITY APPLN. INFO: US 1992-881104 19920511; US  
 1993-14922 19930208  
 REFERENCE PATENTS: 3.Jnl.Ref; EP 368406; EP 399432; EP 452837; JP 02202813;  
 WO 9205811; WO 9308841

## INT. PATENT CLASSIF.:

MAIN: A61K009-70  
 SECONDARY: A61K047-10; A61K047-14

## BASIC ABSTRACT:

WO 9323019 A UPAB: 19941102

Transdermal delivery device for admin. of a drug (I) through the skin for a sustained period comprises: (a) a (I)-impermeable backing layer, forming the upper surface of the device in use; (b) a reservoir layer laminated to (a) containing (I) and a permeation enhancer compsn. comprising a lower aliphatic carboxylic acid lower aliphatic ester (II); (c) a release controller which controls the flow of (I) but not (II) and (III) from the device; and (d) device for retaining the device on the skin to supply (I)-(III). Release controller (c) pref. consists of a membrane in the flow path from reservoir (b) to the skin. A drug delivery method using the device is also claimed.

USE/ADVANTAGE - (I) is pref. timolol (beta-blockers) buprenorphine or nalbuphine (narcotic analgesic) or especially captopril (Ia) (ACE inhibitor). (II) and (III) have synergistic permeation enhancing effect. Membranes (c) do not limit the rate of enhance delivery (i.e. delivery of solvent is skin-controlled), but provide steady-state flux of (I) from the device (i.e. (I) release is system-controlled).

Dwg.0/11

Dwg.0/11

FILE SEGMENT: CPI  
 FIELD AVAILABILITY: AB; DCN

MANUAL CODES: CPI: A12-V01; A12-V03A; B04-A04; B04-C03D; B07-D03;  
 B07-E03; B07-F03; B10-E04C; B10-E04D; B10-G02;  
 B12-C05; B12-D01; B12-E06B; B12-F05A;  
 B12-M02F; B12-M10A

L264 ANSWER 59 OF 63 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN  
 ACCESSION NUMBER: 1993-044798 [05] WPIX  
 DOC. NO. CPI: C1993-020229  
 TITLE: Drug delivery system for increased flux to  
 gastrointestinal tract - comprising semi-permeable wall  
 with areas of increased fluid flux, for anti-ulcer drugs,  
 ACE inhibitors, calcium channel blockers etc..  
 DERWENT CLASS: A96 B07  
 INVENTOR(S): CARPENTER, H A; GUITTARD, G V; HAMEL, L G; QUAN, E S;  
 WONG, P S; WONG, P S L  
 PATENT ASSIGNEE(S): (ALZA) ALZA CORP  
 COUNTRY COUNT: 26  
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN	IPC
US 5178867	A	19930112	(199305)*		10	A61K009-22	
WO 9303711	A1	19930304	(199311)	EN	29	A61K009-20	
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL SE							
W: AU CA FI JP KR NO							
AU 9225449	A	19930316	(199328)			A61K009-20	
ZA 9206241	A	19931229	(199405)		28	A61K000-00	
NO 9400376	A	19940207	(199417)			A61K009-22	
FI 9400787	A	19940218	(199418)			A61K000-00	
PT 100789	A	19940531	(199421)			G03B017-52	
EP 600033	A1	19940608	(199422)	EN		A61K009-20	
R: AT BE CH DE DK ES FR GB GR IE IT LI LU NL SE							
JP 06509809	W	19941102	(199503)			A61K009-00	
NZ 244009	A	19950224	(199513)			A61K009-20	
EP 600033	B1	19951025	(199547)	EN	12	A61K009-20	
R: AT BE CH DE DK ES FR GB GR IE IT LI LU NL SE							
DE 69205687	E	19951130	(199602)			A61K009-20	
ES 2079206	T3	19960101	(199608)			A61K009-20	
AU 666674	B	19960222	(199620)			A61K009-22	
JP 2934505	B2	19990816	(199938)		9	A61K009-00	
CA 2112679	C	20030415	(200330)	EN		A61K009-22	

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 5178867	A	US 1991-747899	19910819
WO 9303711	A1	WO 1992-US7034	19920819
AU 9225449	A	AU 1992-25449	19920819
ZA 9206241	A	ZA 1992-6241	19920819
NO 9400376	A	WO 1992-US7034	19920819
		NO 1994-376	19940207
FI 9400787	A	WO 1992-US7034	19920819
		FI 1994-787	19940218
PT 100789	A	PT 1992-100789	19920819
EP 600033	A1	EP 1992-919273	19920819
		WO 1992-US7034	19920819
JP 06509809	W	WO 1992-US7034	19920819
		JP 1993-504590	19920819
NZ 244009	A	NZ 1992-244009	19920819

EP 600033	B1	EP 1992-919273	19920819
		WO 1992-US7034	19920819
DE 69205687	E	DE 1992-605687	19920819
		EP 1992-919273	19920819
		WO 1992-US7034	19920819
ES 2079206	T3	EP 1992-919273	19920819
AU 666674	B	AU 1992-25449	19920819
JP 2934505	B2	WO 1992-US7034	19920819
		JP 1993-504590	19920819
CA 2112679	C	CA 1992-2112679	19920819
		WO 1992-US7034	19920819

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 9225449	A Based on	WO 9303711
EP 600033	A1 Based on	WO 9303711
JP 06509809	W Based on	WO 9303711
EP 600033	B1 Based on	WO 9303711
DE 69205687	E Based on	EP 600033
	Based on	WO 9303711
ES 2079206	T3 Based on	EP 600033
AU 666674	B Previous Publ.	AU 9225449
	Based on	WO 9303711
JP 2934505	B2 Previous Publ.	JP 06509809
	Based on	WO 9303711
CA 2112679	C Based on	WO 9303711

PRIORITY APPLN. INFO: US 1991-747899 19910819  
 REFERENCE PATENTS: 2.Jnl.Ref; EP 247709; EP 317274; EP 339811; GB 2166052;  
 GB 2167972; US 4519801

## INT. PATENT CLASSIF.:

MAIN: A61K000-00; A61K009-00; A61K009-20; A61K009-22;  
 G03B017-52

SECONDARY: A61K009-32; A61K009-36; A61K031-34; A61K031-415;  
 A61K031-425; A61K031-44; C08L001-10; C08L039-06

## BASIC ABSTRACT:

US 5178867 A UPAB: 19931119

Method comprises administering a drug in up to 8 hours using a dosage form, which comprises: (i) a semipermeable wall permeable to the passage of fluid; surrounding (ii) a compartment containing the drug; and (iii) a passageway in the wall for delivery of the drug and (iv) means in the wall for increasing fluid flux into the dosage form, comprising 40-55% of the wall; also claimed is a compsn. comprising: (a) 40-60% cellulose acylate; (b) 40-55% polyvinylpyrrolidone (PVP) having m.weight 38000-45000; and (c) 0-5% plasticiser; useful for mfr. of an orally administerable dosage form.

USE/ADVANTAGE - The improved dosage form provides osmotically controlled delivery of an orally admin. drug only in the stomach and small intestine, avoiding wastage and possible side effects, from uncontrolled deliveries or throughout the gastrointestinal (GI) tract. The drugs include anti-ulcer drugs (both histamine receptor antagonist or hydrión suppressant types), calcium influx inhibitors (CII) to reduce influx of calcium ions into cardiac and smooth muscles, and angiotensin converting enzyme inhibitor (ACEI), all claimed as delivery methods

Dwg.0/4

FILE SEGMENT: CPI

FIELD AVAILABILITY: AB; DCN

MANUAL CODES: CPI: A03-A03; A04-D05; A07-A01; A12-V01; A12-W11A;  
 B04-C02A3; B04-C03A; B12-F05A; B12-F05B;

## B12-L04; B12-M02F

L264 ANSWER 60 OF 63 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN  
 ACCESSION NUMBER: 1990-084867 [12] WPIX  
 DOC. NO. NON-CPI: N1990-065504  
 DOC. NO. CPI: C1990-037161  
 TITLE: Transdermal antihypertensive compsn. - containing  
 (R)-3-((S)-1-carboxy-5-(4-piperidyl) pentyl) amino-4-oxo-  
 2,3,4,5-tetra hydro-1,5-benzothiazepine -5-acetic acid.  
 DERWENT CLASS: B02 P34  
 INVENTOR(S): NISHIKAWA, K; NONOMURA, M; YAMADA, M  
 PATENT ASSIGNEE(S): (TAKE) TAKEDA CHEM IND LTD  
 COUNTRY COUNT: 14  
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN	IPC
EP 359004	A	19900321	(199012)*	EN	9		
R: AT BE CH DE FR GB IT LI LU NL SE							
AU 8940937	A	19900308	(199019)				
DK 8904295	A	19900306	(199021)				
JP 02174716	A	19900706	(199033)				

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 359004	A	EP 1989-115687	19890825
JP 02174716	A	JP 1989-228491	19890904

PRIORITY APPLN. INFO: JP 1988-222081 19880905  
 REFERENCE PATENTS: 2.Jnl.Ref; EP 156455  
 INT. PATENT CLASSIF.: A61K009-70; A61K031-55; A61K047-00; A61L015-16  
 BASIC ABSTRACT:

EP 359004 A UPAB: 19930928  
 Transdermal therapeutic compsn. contains: (i) (R)-3-((S)-1-carboxy  
 5-(4-piperidyl)pentyl) amino-4-oxo-2,3,4,5-tetrahydro -1,5-benzothiazepine-  
 5-acetic acid; (ii) an inorganic base; (iii) at least one member selected  
 from (a) 6-20C aliphatic carboxylic acid, (b) lower alcohol ester of 6-20C  
 aliphatic acid and (c) a 6-20C aliphatic alcohol; and (iv) an alkane  
 polyol.

USE/ADVANTAGE - Compound (i) is a known ACE inhibitor. The compsn. is  
 useful for the prophylactic or therapeutic treatment of hypertension. The  
 compsn. is in a dosage form of patch, cataplasma, ointment, hard ointment,  
 tape, suppository, lotion, solution suspension, emulsion or aerosol. The  
 therapeutic formulation comprises the compsn. and a solvent, a suspending  
 agent, an emulsifier, a propellant, an ointment base or a suppository. The  
 therapeutic agent contains the compsn. absorbed in or adhered to  
 appropriate support material. The formulation gives enhanced absorption  
 and duration of action with reduced dermal irritation potential. Component  
 (i) is used in an amount of 5-30 mg in the compsn. Pref. once a day.

0/0

FILE SEGMENT: CPI GMPI  
 FIELD AVAILABILITY: AB; DCN  
 MANUAL CODES: CPI: B06-F03; B10-C04E; B10-E04C; B10-E04D; B10-G02;  
 B12-F05A; B12-M02F

L264 ANSWER 61 OF 63 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN  
 ACCESSION NUMBER: 1989-332134 [45] WPIX

CROSS REFERENCE: 1986-293057 [45]; 1990-044743 [06]; 1991-001272 [01];  
 1991-101854 [14]; 1991-101855 [14]; 1991-101879 [14];  
 1992-267899 [32]; 1997-022764 [03]; 1997-449091 [42]  
 DOC. NO. CPI: C1989-147221  
 TITLE: Drug-containing lollipop for trans-mucosal delivery -  
 comprises matrix of soluble, compressible carbohydrate.  
 DERWENT CLASS: B05 B07 P33  
 INVENTOR(S): HAGUE, B; STANLEY, T H  
 PATENT ASSIGNEE(S): (ANES-N) ANESTA CORP; (UTAH) UNIV UTAH  
 COUNTRY COUNT: 15  
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN	IPC
US 4863737	A	19890905	(198945)*		20		
WO 9103099	A	19910307	(199112)#				
RW: AT BE CH DE FR GB IT LU NL SE							
W: AU DK JP NO							
AU 8940704	A	19910403	(199125)#				
NO 9200565	A	19920213	(199222)#			A61K009-00	
JP 05501539	W	19930325	(199317)		16	A61K009-00	

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
US 4863737	A	US 1987-60045	19870608
JP 05501539	W	JP 1989-504878	19890816
		WO 1989-US3518	19890816

## FILING DETAILS:

PATENT NO	KIND	PATENT NO
JP 05501539	W Based on	WO 9103099

PRIORITY APPLN. INFO: US 1987-60045 19870608; US  
 1985-729301 19850501

REFERENCE PATENTS: US 2926121; US 4551329; US 4695463; US 4749575; US  
 4764378

INT. PATENT CLASSIF.: A61K009-20; A61K009-68; A61K047-36; H02M003-33  
 MAIN: A61K009-00

SECONDARY: A61K009-20; A61K009-68; A61K047-36; H02M003-33

## BASIC ABSTRACT:

US 4863737 A UPAB: 19981210

Drug-containing lollipop for use in transmucosal drug delivery comprises a matrix of soluble, compressible carbohydrate containing a uniform dispersion of a pharmacologically effective dose of a powdered drug which is capable of absorption through the mucosa of the mouth, pharynx and oesophagus, the dispersion being formed at a temperature below the m.pt. of the drug and carbohydrate and compressed to form a solid integral mass which is attached to a holder.

ADVANTAGE - The drug reaches the bloodstream almost as quickly as through injection, and much more quickly than by oral admin. Problems associated with oral or i.v. admin. can be reduced, e.g. difficulty in swallowing pills, rapid metabolism of certain (e.g. CNS or cardiovascular acting) drugs in the liver, the need for repeated injections of low doses in order to avoid overdosing, etc.

Dwg.0/5

FILE SEGMENT: CPI GMPI

FIELD AVAILABILITY: AB; DCN  
 MANUAL CODES: CPI: B04-C02; B06-A02; B06-D04; B07-H; B12-A02C; B12-C04;  
 B12-D01; B12-D05; B12-E09; B12-F01C; B12-F02;  
**B12-F05A**; B12-G01B3; B12-G03; B12-H05;  
 B12-J02; B12-K02; **B12-M02F**; B12-M11

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 ACCESSION NUMBER: 1989-280855 [39] WPIX  
 DOC. NO. CPI: C1989-124251  
 TITLE: Drug used as therapeutic agent of hypertension - contains  
 3-amino-4-oxo-2,3,4,5-tetra hydro-1,5-benzothiazepine-5-  
 acetic acid and lactic acid and/or urease by overriding  
 actuator.  
 DERWENT CLASS: A96 B02  
 PATENT ASSIGNEE(S): (TAKE) TAKEDA CHEM IND LTD  
 COUNTRY COUNT: 1  
 PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN	IPC
JP 01203328	A	19890816	(198939)*		8		

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
JP 01203328	A	JP 1988-28246	19880209

PRIORITY APPLN. INFO: JP 1988-28246 19880209  
 INT. PATENT CLASSIF.: A61K009-08; A61K031-55; C07D417-12  
 BASIC ABSTRACT:

JP 01203328 A UPAB: 19930923

Liquid mixture contains (i) (R)-3-((S)-1-carboxy-5-(4-piperidyl)  
 pentyl)amino-4-oxo-2,3,4,5-tetrahydro -1,5-benzothiazepine-5-acetic of  
 formula (I), and (ii) lactic acid and/or urine.

Specifically, the cpd. (I) is formed into a tape ointment, lotion or  
 cream. The amount for dissolving in lactic acid solution is 0.1-30% (W/W),  
 especially

1-20% (W/W). The cpd. (I) is dissolved in an urine solution containing 1-60%  
 (W/W) with an amount of 0.1-17.5% (W/V), especially 1-15% (W/V) of cpd. (I). The  
 dose of cpd. (I) is 1-200 mg, especially 10-30 mg/day for 1-7 days. The  
 therapeutic drug opt. contains other additives, e.g. polybasic alcohol,  
 e.g. propylene glycol, 1,3-butylene glycol, or glycerine; saccharides e.g.  
 sorbitol; surfactants, e.g. Tween 80 or Span 60 (RTM); water-soluble  
 polymers, e.g. polyvinylpyrrolidone or polyvinyl-alcohol; fatty acids,  
 e.g. oleic acid, oleyl alcohol; vegetable oil (olive oil or jojoba oil) or  
 mineral oil (e.g. paraffin or vaseline).

USE/ADVANTAGE - Cpd. (I) has angiotensin converting enzyme inhibitor  
 activity. The drug is a therapeutic agent of hypertension.

0/0

FILE SEGMENT: CPI  
 FIELD AVAILABILITY: AB; DCN  
 MANUAL CODES: CPI: A12-V01; B06-F03; B10-A13C; B10-C04D;  
**B12-F05A**; **B12-M02F**

L264 ANSWER 63 OF 63 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN  
 ACCESSION NUMBER: 1988-133133 [19] WPIX  
 DOC. NO. CPI: C1988-059570  
 TITLE: New mixed organic acid anhydride(s) - formed from acid

DERWENT CLASS: having, e.g. antiinflammatory, anti-epileptic, biocidal, cytostatic, diuretic, activity, or steroid acid.  
 INVENTOR(S): B05  
 PATENT ASSIGNEE(S): DECOCK, E J; JANSEN, F H  
 COUNTRY COUNT: (GANT-N) GANTAX PHARM NV; (JANS-I) JANSEN F H J  
 PATENT INFORMATION: 15

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN	IPC
WO 8803020	A	19880505	(198819)*	EN	21		
RW: AT BE CH DE FR GB IT LU NL SE							
W: DK JP KR US							
NL 8602767	A	19880516	(198824)				
DK 8803465	A	19880623	(198846)				
EP 293432	A	19881207	(198849)	EN			
R: AT BE CH DE FR GB IT LI LU NL SE							
JP 01501625	W	19890608	(198929)				

## APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 8803020	A	WO 1987-EP664	19871030
NL 8602767	A	NL 1986-2767	19861031
EP 293432	A	EP 1988-900014	19871030
JP 01501625	W	JP 1988-500378	19861031

PRIORITY APPLN. INFO: NL 1986-2767 19861031  
 REFERENCE PATENTS: DE 2126037; EP 88252; US 3686183; US 4158012; US 4570017;  
 GB 1388265  
 INT. PATENT CLASSIF.: A61K031-18; C07C057-30; C07C065-21; C07C079-46;  
 C07C101-45; C07C103-46; C07D213-89; C07D215-06;  
 C07K005-06

## BASIC ABSTRACT:

WO 8803020 A UPAB: 19990624  
 Mixed organic acid anhydrides of formula R1-CO-O-CO-R2 (I) and their salts are new. (R1 = the residue of an organic acid having anti-inflammatory, anti-epileptic, ACE-inhibiting, biocidal, cytostatic, diuretic, antidiarrheal or cerebrotentorial activity or of a steroid acid; R2 is different from R1 and represents -CR3R4R5, a steroid fragment or an amino acid or peptide moiety; R3, R4, R5 = H, or a 1-20C -alkyl or -alkenyl, cycloalkyl or -alkenyl, aryl, aralkyl, aralkyl gp., opt. subst. by alkyl, aryl, alkoxy, aryloxy, alkoxy carbonyl or aryloxy carbonyl and opt. containing one or more heteroatoms).

USE/ADVANTAGE - Hydrolysis of (I) to the pharmacologically active cpd. is not dependent on the action of enzymes, thereby permitting the adjustment of the degree of hydrolysability in vivo by selecting for a given R1-group a suitable R2 gp. Inherent to the anhydride form, into which the medicine is converted, is a decreased polarity and acidity and an increased lipophilicity. This reduces the irritation of the gastro-intestinal system in the case of oral intake and the ability to be absorbed by the skin increases such as with transdermal and transmucosal absorption.

Dwg.0/1

FILE SEGMENT: CPI  
 FIELD AVAILABILITY: AB  
 MANUAL CODES: CPI: B01-D02; B06-H; B07-H; B10-A10; B10-A23; B10-A25;  
 B12-A01; B12-A06; B12-C06; B12-D04; B12-D07;

B12-F05A; B12-G03; B12-J04; B12-M02F

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